2021

ANNUAL REPORT

REGENERON

REGENERON BY THE NUMBERS

30+
investigational medicines in clinical development

146
global and U.S. patient advocacy and professional societies engaged across 28 diseases

clinical trials in
55+
COUNTRIES

offices in
6
COUNTRIES
(U.S., Ireland, England, Canada, Germany and the Netherlands)

9
FDA-approved medicines

12K+
hours of Regeneron volunteer service to local communities during fifth annual *Day for Doing Good*

~2M
exomes sequenced by the Regeneron Genetics Center®

40M+
doses of EYLEA® (aflibercept) Injection administered worldwide since launch 10 years ago

2.8M
doses of REGEN-COV® (casirivimab and imdevimab) delivered to U.S. government

85
active molecules managed by Industrial Operations and Product Supply

670K
students participated in STEM programs provided by Regeneron

9 OUT OF 10
employees say Regeneron is a great place to work

FORM 10-K

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number: 0-19034

REGENERON PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

New York	**13-3444607**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

777 Old Saw Mill River Road Tarrytown, New York 10591-6707
(Address of principal executive offices, including zip code)

(914) 847-7000
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	*Trading Symbol*	*Name of each exchange on which registered*
Common Stock - par value $.001 per share	**REGN**	**NASDAQ Global Select Market**

Securities registered pursuant to section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant was approximately $57,065,000,000, computed by reference to the closing sales price of the stock on NASDAQ on June 30, 2021, the last trading day of the registrant's most recently completed second fiscal quarter. For purposes of this calculation only, the registrant has assumed that all of its directors and executive officers, and no other persons, are its affiliates. This determination of affiliate status is not necessarily a determination for other purposes.

The number of shares outstanding of each of the registrant's classes of common stock as of January 27, 2022:

Class of Common Stock	Number of Shares
Class A Stock, $.001 par value	1,823,283
Common Stock, $.001 par value	106,715,999

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the Registrant's definitive proxy statement to be filed in connection with solicitation of proxies for its 2022 Annual Meeting of Shareholders are incorporated by reference into Part III of this Form 10-K. Exhibit index is located on pages 95 to 101 of this filing.

REGENERON PHARMACEUTICALS, INC.
ANNUAL REPORT ON FORM 10-K
TABLE OF CONTENTS

PART I

ITEM 1. BUSINESS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. (where applicable, together with its subsidiaries, "Regeneron," "Company," "we," "us," and "our"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation EYLEA® (aflibercept) Injection, Dupixent® (dupilumab) Injection, Libtayo® (cemiplimab) Injection, Praluent® (alirocumab) Injection, Kevzara® (sarilumab) Injection, Evkeeza® (evinacumab), Inmazeb® (atoltivimab, maftivimab, and odesivimab-ebgn), REGEN-COV® (casirivimab and imdevimab), aflibercept 8 mg, fasinumab, pozelimab, odronextamab, itepekimab, REGN5458, REGN5713-5714-5715, REGN1908-1909, Regeneron's other oncology programs (including its costimulatory bispecific portfolio), Regeneron's and its collaborators' earlier-stage programs, and the use of human genetics in Regeneron's research programs; the likelihood and timing of achieving any of our anticipated development milestones referenced in this report; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; the likelihood, timing, and scope of possible regulatory approval and commercial launch of our late-stage product candidates and new indications for Regeneron's Products, including without limitation those listed above; the extent to which the results from the research and development programs conducted by us and/or our collaborators may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict our ability to continue to develop or commercialize Regeneron's Products and Regeneron's Product Candidates; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) or recommendations and guidelines from governmental authorities and other third parties on the commercial success of Regeneron's Products and Regeneron's Product Candidates; our ability to manufacture and manage supply chains for multiple products and product candidates; the ability of our collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the availability and extent of reimbursement of Regeneron's Products from third-party payors, including private payor healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payors and new policies and procedures adopted by such payors; unanticipated expenses; the costs of developing, producing, and selling products; our ability to meet any of our financial projections or guidance, including without limitation capital expenditures, and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including our agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as Regeneron's agreement with Roche relating to the casirivimab and imdevimab antibody cocktail (known as REGEN-COV in the United States and Ronapreve™ in other countries), to be cancelled or terminated; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA, Dupixent, Praluent, and REGEN-COV described further in Note 15 to our Consolidated Financial Statements included in this report), other litigation and other proceedings and government investigations relating to the Company and/or its operations (including without limitation those described in Note 15 to our Consolidated Financial Statements included in this report), the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on our business, prospects, operating results, and financial condition. These statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any such statements. In evaluating such statements, shareholders and potential investors should specifically consider the various factors identified under Part I, Item 1A. "Risk Factors," which could cause actual events and results to differ materially from those indicated by such forward-looking statements. We do not undertake any obligation to update (publicly or otherwise) any forward-looking statement, whether as a result of new information, future events, or otherwise.

General

Regeneron Pharmaceuticals, Inc. is a fully integrated biotechnology company that discovers, invents, develops, manufactures, and commercializes medicines for serious diseases. Our commercialized medicines and product candidates in development are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematologic conditions, infectious diseases, and rare diseases.

Our core business strategy is to maintain a strong foundation in basic scientific research and discovery-enabling technologies, and to build on that foundation with our clinical development, manufacturing, and commercial capabilities. Our objective is to continue to be an integrated, multi-product biotechnology company that provides patients and medical professionals with important options for preventing and treating human diseases.

Selected financial information is summarized as follows:

	Year Ended December 31,		
(In millions, except per share data)	**2021**	**2020**	**2019**
Revenues	$16,071.7	$ 8,497.1	$ 6,557.6
Net income	$ 8,075.3	$ 3,513.2	$ 2,115.8
Net income per share - diluted	$ 71.97	$ 30.52	$ 18.46

For purposes of this report, references to our products encompass products marketed or otherwise commercialized by us and/or our collaborators or licensees and references to our product candidates encompass product candidates in development by us and/or our collaborators or licensees (in the case of collaborated or licensed products or product candidates under the terms of the applicable collaboration or license agreements), unless otherwise stated or required by the context.

Products

Products that have received marketing approval are summarized in the table below.

		Territory			
Product	**Disease**	**U.S.**	**EU**	**Japan**	**ROW[4]**
EYLEA (aflibercept) Injection[1]	- Neovascular age-related macular degeneration ("wet AMD")	✔	✔	✔	✔
	- Diabetic macular edema ("DME")	✔	✔	✔	✔
	- Macular edema following retinal vein occlusion ("RVO"), which includes macular edema following central retinal vein occlusion ("CRVO") and macular edema following branch retinal vein occlusion ("BRVO")	✔	✔	✔	✔
	- Myopic choroidal neovascularization ("mCNV")		✔	✔	✔
	- Diabetic retinopathy	✔			
	- Neovascular glaucoma ("NVG")			✔	
Dupixent (dupilumab) Injection[2]	- Atopic dermatitis (in adults and adolescents)	✔	✔	✔	✔
	- Atopic dermatitis (in pediatrics 6–11 years of age)	✔	✔		✔
	- Asthma (in adults and adolescents)	✔	✔	✔	✔
	- Asthma (in pediatrics 6–11 years of age)	✔			
	- Chronic rhinosinusitis with nasal polyposis ("CRSwNP")	✔	✔	✔	✔

Product *(continued)*	Disease	Territory			
		U.S.	EU	Japan	ROW[4]
Libtayo (cemiplimab) Injection[2]	- Metastatic or locally advanced first-line non-small cell lung cancer ("NSCLC")	✔	✔		✔
	- Metastatic or locally advanced basal cell carcinoma ("BCC")	✔	✔		✔
	- Metastatic or locally advanced cutaneous squamous cell carcinoma ("CSCC")	✔	✔		✔
Praluent (alirocumab) Injection[3]	- LDL-lowering in heterozygous familial hypercholesterolemia ("HeFH") or clinical atherosclerotic cardiovascular disease ("ASCVD")	✔	✔		✔
	- Cardiovascular risk reduction in patients with established cardiovascular disease	✔	✔		✔
	- Homozygous familial hypercholesterolemia ("HoFH")	✔			
REGEN-COV[5]	- COVID-19		✔	✔	✔
Kevzara (sarilumab) Solution for Subcutaneous Injection[2]	- Rheumatoid arthritis ("RA")	✔	✔	✔	✔
Evkeeza (evinacumab) Injection[6]	- HoFH (in adults and adolescents)	✔	✔		
Inmazeb (atoltivimab, maftivimab, and odesivimab-ebgn) Injection	- Infection caused by *Zaire ebolavirus*	✔			
ARCALYST® (rilonacept) Injection for Subcutaneous Use[7]	- Cryopyrin-associated periodic syndromes ("CAPS"), including familial cold auto-inflammatory syndrome ("FCAS") and Muckle-Wells syndrome ("MWS") (in adults and adolescents)	✔			
	- Deficiency of interleukin-1 receptor antagonist ("DIRA") (in adults and pediatrics)	✔			
	- Recurrent pericarditis (in adults and adolescents)	✔			
ZALTRAP® (ziv-aflibercept) Injection for Intravenous Infusion[8]	- Metastatic colorectal cancer ("mCRC")	✔	✔	✔	✔

Note: Refer to "Net Product Sales of Regeneron-Discovered Products" section below for information regarding whether net product sales for a particular product are recorded by us or others. In addition, unless otherwise noted, products in the table above are approved for use in adults in the above-referenced diseases.

(1) In collaboration with Bayer outside the United States

(2) In collaboration with Sanofi

(3) Pursuant to a 2020 agreement, the Company is solely responsible for the development and commercialization of Praluent in the United States, and Sanofi is solely responsible for the development and commercialization of Praluent outside of the United States (and Sanofi pays us a royalty on net product sales of Praluent outside the United States).

(4) Rest of world ("ROW"). A checkmark in this column indicates that the product has received marketing approval in at least one country outside of the United States, European Union ("EU"), or Japan.

(5) Known as REGEN-COV in the United States and Ronapreve in other countries

(6) In January 2022, the Company entered into a license and collaboration agreement for Ultragenyx to develop and commercialize Evkeeza outside of the United States. Ultragenyx pays us a percentage of net product sales of Evkeeza outside the United States and the Company is also eligible to receive regulatory and sales milestone payments.

[7] Pursuant to a 2017 license agreement with Kiniksa, we granted Kiniksa the right to develop and commercialize certain new indications for ARCALYST. In March 2021, Kiniksa received marketing approval for its first new indication of ARCALYST in the United States; consequently we granted U.S. commercial rights to ARCALYST for all previously approved indications and Kiniksa pays us a share of ARCALYST profits.

[8] Sanofi is solely responsible for the development and commercialization of ZALTRAP, and Sanofi pays us a percentage of aggregate net product sales of ZALTRAP.

REGEN-COV - Emergency and Temporary Use Authorizations

In November 2020, the antibody cocktail casirivimab and imdevimab administered together, known as REGEN-COV in the United States, received Emergency Use Authorization ("EUA") from the U.S. Food and Drug Administration ("FDA") for the treatment of mild to moderate COVID-19 in adults, as well as in pediatric patients at least 12 years of age and weighing at least 40 kg, who have received positive results of direct SARS-CoV-2 viral testing and are at high risk for progressing to severe COVID-19 and/or hospitalization.

The EUA is temporary and does not replace a formal Biologics License Application ("BLA") submission review and approval process. This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use, unless terminated or revoked sooner.

In June 2021, the FDA updated the EUA for REGEN-COV, lowering the dose to 1,200 mg (which is half the dose originally authorized) and allowing for subcutaneous injections as an alternative when intravenous ("IV") infusion is not feasible and would lead to a delay in treatment. In July 2021, the FDA also expanded the EUA to include post-exposure prophylaxis in people at high risk for progression to severe COVID-19, who are not fully vaccinated or are not expected to mount an adequate response to vaccination, and who have been exposed to a SARS-CoV-2 infected individual or are at high risk of exposure to an infected individual because of infection occurring in the same institutional setting (such as in nursing homes or prisons).

Based on laboratory data that showed markedly decreased binding to the Omicron spike protein, REGEN-COV is highly unlikely to be active against the Omicron variant. In January 2022, the FDA revised the EUA for REGEN-COV to exclude its use in geographic regions where, based on available information including variant susceptibility and regional variant frequency, infection or exposure is likely due to a variant such as Omicron (B.1.1.529) that is not susceptible to the treatment. With this EUA revision, REGEN-COV is not currently authorized for use in any U.S. states, territories, or jurisdictions, since Omicron is currently the dominant variant across the United States. If, in the future, patients in certain geographic regions are likely to be infected or exposed to a variant that is susceptible to REGEN-COV, then the limitation on use may be revised in these areas.

Emergency or temporary pandemic use authorizations are also currently in place in numerous other countries outside the United States.

Net Product Sales of Regeneron-Discovered Products

	Year Ended December 31,								
	2021			2020			2019		
(In millions)	U.S.	ROW	Total	U.S.	ROW	Total	U.S.	ROW	Total
EYLEA[(a)]	$5,792.3	$3,592.4	$9,384.7	$4,947.2	$2,961.5	$7,908.7	$4,644.2	$2,897.4	$7,541.6
Dupixent[(b)]	$4,713.0	$1,485.3	$6,198.3	$3,226.2	$ 818.6	$4,044.8	$1,871.2	$ 444.4	$2,315.6
Libtayo[(c)]	$ 306.3	$ 151.9	$ 458.2	$ 270.7	$ 77.5	$ 348.2	$ 175.7	$ 18.1	$ 193.8
Praluent[(d)]	$ 170.0	$ 251.1	$ 421.1	$ 186.0	$ 172.8	$ 358.8	$ 126.0	$ 162.7	$ 288.7
REGEN-COV[(e)]	$5,828.0	$1,745.9	$7,573.9	$ 185.7	—	$ 185.7	—	—	—
Kevzara[(b)]	$ 161.9	$ 176.1	$ 338.0	$ 141.6	$ 128.3	$ 269.9	$ 129.0	$ 77.7	$ 206.7
Evkeeza[(f)]	$ 18.4	—	$ 18.4	—	—	—	—	—	—
ARCALYST[(g)]	$ 2.2	—	$ 2.2	$ 13.1	—	$ 13.1	$ 14.5	—	$ 14.5
ZALTRAP[(b)]	$ 5.3	$ 86.4	$ 91.7	$ 5.8	$ 97.9	$ 103.7	$ 7.3	$ 101.1	$ 108.4

[(a)] Regeneron records net product sales of EYLEA in the United States. Bayer records net product sales of EYLEA outside the United States. The Company records its share of profits/losses in connection with sales of EYLEA outside the United States.

[(b)] Sanofi records global net product sales of Dupixent, Kevzara, and ZALTRAP. The Company records its share of profits/losses in connection with global sales of Dupixent and Kevzara, and Sanofi pays the Company a percentage of net sales of ZALTRAP.

[(c)] Regeneron records net product sales of Libtayo in the United States and Sanofi records net product sales of Libtayo outside the United States. The parties equally share profits/losses in connection with global sales of Libtayo.

[(d)] Effective April 1, 2020, Regeneron records net product sales of Praluent in the United States. Also effective April 1, 2020, Sanofi records net product sales of Praluent outside the United States and pays the Company a royalty on such sales. Previously, Sanofi recorded global net product sales of Praluent and the Company recorded its share of profits/losses in connection with such sales. Refer to "Collaboration, License, and Other Agreements - Sanofi" section below for further details.

[(e)] Regeneron records net product sales of REGEN-COV in connection with its agreements with the U.S. government. Roche records net product sales of the antibody cocktail outside the United States and the parties share gross profits from global sales based on a pre-specified formula. Refer to "Agreements Related to COVID-19" below for further details.

[(f)] Regeneron records net product sales of Evkeeza in the United States. Pursuant to the January 2022 agreement, Ultragenyx will record net product sales of Evkeeza outside of the United States and will pay the Company a percentage of such sales. Refer to "Products" section above and "Collaboration, License, and Other Agreements - Ultragenyx" section below for further details.

[(g)] Amounts reflected in the table above represent net product sales recorded by Regeneron. Effective April 1, 2021, Kiniksa records net product sales of ARCALYST in the United States and pays us a share of ARCALYST profits, if any. Refer to "Products" section above and "Collaboration, License, and Other Agreements - Kiniksa" section below for further details.

Programs in Clinical Development

Product candidates in clinical development, which are being developed by us and/or our collaborators, are summarized in the table below.

There are numerous uncertainties associated with drug development, including uncertainties related to safety and efficacy data from each phase of drug development (including any post-approval studies), uncertainties related to the enrollment and performance of clinical trials, changes in regulatory requirements, changes to drug pricing and reimbursement regulations and requirements, and changes in the competitive landscape affecting a product candidate. The planning, execution, and results of our clinical programs are significant factors that can affect our operating and financial results.

We and our collaborators conduct clinical trials in multiple countries across the world. The COVID-19 pandemic and the restrictions adopted around the globe to reduce the spread of the disease have impacted and may continue to impact our clinical development programs. We continue to evaluate the impact of the COVID-19 pandemic on an individual trial basis and oversee trial management while also working to ensure patient safety and provide sufficient supply of product candidates for the studies. The ultimate impact (including possible delays in recruiting and/or obtaining data) resulting from the COVID-19 pandemic will depend, among other factors, on the extent of the pandemic in the areas with study sites and patient populations. It is possible that the COVID-19 pandemic may cause clinical disruptions beyond those we have described. In addition, there may be delays in the timing of regulatory review and other projected milestones discussed in the table below.

Refer to Part I, Item 1A. "Risk Factors" for a description of these and other risks and uncertainties that may affect our clinical programs, including those related to the COVID-19 pandemic.

Clinical Program	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
Ophthalmology						
EYLEA (aflibercept)[b]			–Retinopathy of prematurity ("ROP")[c]	–ROP (EU and Japan)	–Initial results from National Institutes of Health ("NIH")-sponsored Protocol W trial in non-proliferative diabetic retinopathy ("NPDR") were announced; data confirmed results from Company-sponsored PANORAMA trial and demonstrated reduced risk of developing vision-threatening complications with every-16-weeks dosing regimen –Completed enrollment in Phase 3 study for ROP	–Submit supplemental BLA ("sBLA") for every-16-weeks dosing regimen in patients with NPDR (first half 2022) –Report results from Phase 3 study in ROP (second half 2022)
Aflibercept 8 mg[b]		–Wet AMD	–Wet AMD –DME		–Completed enrollment in Phase 3 studies in wet AMD and DME –Reported initial data from Phase 2 trial in wet AMD and that trial met its primary safety and efficacy endpoints	–Report detailed results from Phase 2 trial in wet AMD (first quarter 2022) –Report results from Phase 3 studies in wet AMD and DME (second half 2022)
Immunology & Inflammation						
Dupixent (dupilumab)[a] *Antibody to IL-4R alpha subunit*		–Peanut allergy –Grass allergy	–Atopic dermatitis in pediatrics (6 months–5 years of age) (Phase 2/3)[d] –Eosinophilic esophagitis ("EoE")[c] in adults[d], adolescents[d], and pediatrics	–Atopic dermatitis in pediatrics (6 months–5 years of age) (U.S.) –Asthma in pediatrics (6–11 years of age) (EU) –EoE in adults and adolescents (U.S.)	–Reported that Phase 3 trial for atopic dermatitis in pediatrics (6 months–5 years of age) met its primary and key secondary endpoints –Initiated Phase 3 study in hand and foot atopic dermatitis –Approved by FDA for asthma in pediatrics (6–11 years of age)	–FDA decision on sBLA for atopic dermatitis in pediatric patients (6 months–5 years of age) (mid-2022) –Submit regulatory application in the EU for atopic dermatitis in pediatric patients (6 months–5 years of age) (first half 2022)

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
Dupixent (dupilumab)[a] *(continued)*			–Chronic obstructive pulmonary disease ("COPD") –Bullous pemphigoid (Phase 2/3)[c] –Chronic spontaneous urticaria ("CSU") –Prurigo nodularis –Allergic bronchopulmonary aspergillosis ("ABPA") –Chronic inducible urticaria - cold –Chronic rhinosinusitis without nasal polyposis –Allergic fungal rhinosinusitis		–European Medicines Agency's ("EMA") Committee for Medicinal Products for Human Use adopted a positive opinion for severe asthma in pediatrics (6–11 years of age) –*New England Journal of Medicine ("NEJM")* published positive results from Phase 3 trial in pediatrics (6–11 years of age) with moderate-to-severe asthma –Reported that Phase 3 trial in CSU met its primary and key secondary endpoints –Reported that two Phase 3 trials in prurigo nodularis met their respective primary and key secondary endpoints –Reported that Part B of the Phase 3 trial in adults and adolescents with EoE met its co-primary endpoints –Approved by FDA for 200 mg auto-injector –Reported that Phase 2 trial of Dupixent in combination with Aimmune Therapeutics' AR101, an oral immunotherapy, in pediatric patients with peanut allergy met its primary and key secondary endpoint	–European Commission ("EC") decision on regulatory submission for asthma in pediatrics (6–11 years of age) (first half 2022) –Complete rolling sBLA submission for EoE in adults and adolescents (first quarter 2022) –Report results from Phase 2 study in peanut allergy (second half 2022) –Report results from additional Phase 3 CSU study (second half 2022) –Submit sBLA for prurigo nodularis (first half 2022) –Report results from Phase 3 study in chronic inducible urticaria - cold (second half 2022)

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
Kevzara (sarilumab)[a] *Antibody to IL-6R*		–Polyarticular-course juvenile idiopathic arthritis ("pcJIA") –Systemic juvenile idiopathic arthritis ("sJIA")				
Itepekimab[a] **(REGN3500)** *Antibody to IL-33*			–COPD			
REGN1908-1909[f] *Multi-antibody therapy to Fel d 1*			–Cat allergy		–Reported that Phase 2 study in cat allergic patients with mild asthma met its primary and key secondary endpoints	
REGN5713-5714-5715 *Multi-antibody therapy to Bet v 1*			–Birch allergy		–Initial Phase 3 study in birch allergic patients with allergic rhinoconjunctivitis met its primary endpoint	
REGN6490 *Antibody to IL-36R*	–Palmo-plantar pustulosis					
Solid Organ Oncology						
Libtayo (cemiplimab)[a][g] *Antibody to PD-1*		–Metastatic or locally advanced CSCC[d] –Neoadjuvant CSCC –Second-line cervical cancer, ISA101b combination	–First-line NSCLC, chemotherapy combination –Second-line cervical cancer[e] –Adjuvant CSCC	–Second-line cervical cancer (EU) –First-line NSCLC, chemotherapy combination (U.S. and EU)	–Approved by FDA and EC for first-line NSCLC, monotherapy –Approved by FDA and EC for BCC –Reported Phase 3 chemotherapy combination trial in NSCLC met its overall survival primary endpoint; trial stopped early based on Independent Data Monitoring Committee ("IDMC") recommendation	–FDA decision on sBLA (target action date of September 19, 2022) and EC decision on regulatory submission for NSCLC, chemotherapy combination (second half 2022) –EC decision on regulatory submission for cervical cancer (second half 2022)

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
Libtayo (cemiplimab)[a][g] *(continued)*					–Reported positive results from Phase 3 trial in cervical cancer, demonstrating an overall survival benefit; trial stopped early based on IDMC recommendation –Voluntarily withdrew sBLA for cervical cancer due to inability to align with FDA on certain post-marketing studies	
REGN4018[f] *Bispecific antibody targeting MUC16 and CD3*	–Platinum-resistant ovarian cancer					–Report results from Phase 1 study in platinum-resistant ovarian cancer (2022)
REGN5668 *Bispecific antibody targeting MUC16 and CD28*	–Ovarian cancer					
REGN5678 *Bispecific antibody targeting PSMA and CD28*	–Prostate cancer					–Report results from Phase 1 study in prostate cancer (2022)
REGN4336 *Bispecific antibody targeting PSMA and CD3*	–Prostate cancer					
REGN5093 *Bispecific antibody targeting two distinct MET epitopes*	–MET-altered advanced NSCLC					
REGN5093-M114 *Bispecific antibody-drug conjugate targeting two distinct MET epitopes*	–MET overexpressing advanced cancer					
Fianlimab[f] **(REGN3767)** *Antibody to LAG-3*	–Solid tumors and advanced hematologic malignancies				–Presented positive data from Phase 1 trial in combination with Libtayo in advanced melanoma at American Society of Clinical Oncology Annual Meeting	–Initiate Phase 3 study in first-line metastatic melanoma (first half 2022)
REGN6569 *Antibody to GITR*	–Solid tumors					

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
REGN7075 *Bispecific antibody targeting EGFR and CD28*	–Solid tumors					
Hematology						
Odronextamab (REGN1979) *Bispecific antibody targeting CD20 and CD3*	–Certain B-cell malignancies[c]	–B-cell non-Hodgkin lymphoma ("B-NHL") (potentially pivotal study)			–Resumed enrollment of patients with follicular lymphoma ("FL") and diffuse large B-cell lymphoma ("DLBCL") following protocol amendments	–Report additional results from potentially pivotal Phase 2 study in B-NHL (2022) –Initiate Phase 3 program (second half 2022)
REGN5458[f] *Bispecific antibody targeting BCMA and CD3*		–Multiple myeloma (potentially pivotal study)			–Presented results for higher dose level cohorts from Phase 1 trial in multiple myeloma at American Society of Hematology ("ASH") Annual Meeting	–Complete enrollment in potentially pivotal Phase 2 study in multiple myeloma (first quarter 2022) –Report results from potentially pivotal Phase 2 study in multiple myeloma (second half 2022) –Expand into earlier lines of multiple myeloma therapy (first half 2022)
REGN5459[f] *Bispecific antibody targeting BCMA and CD3*	–Multiple myeloma					
Pozelimab[f] (REGN3918) *Antibody to C5; studied as monotherapy and in combination with cemdisiran*		–CD55-deficient protein-losing enteropathy[c], monotherapy (potentially pivotal study)	–Myasthenia gravis, cemdisiran combination[n] –Paroxysmal nocturnal hemoglobinuria ("PNH"), cemdisiran combination[c][n]			–Submit BLA for CD55-deficient protein-losing enteropathy, monotherapy (second half 2022)
Cemdisiran[n] *siRNA therapeutic targeting C5*		–Immunoglobulin A nephropathy				
REGN7257 *Antibody to IL2Rg*	–Aplastic anemia					

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
NTLA-2001[m] *TTR gene knockout using CRISPR/Cas9*	–Transthyretin amyloidosis ("ATTR")[c]				–Reported positive interim data from Phase 1 trial in hereditary transthyretin amyloidosis with polyneuropathy	
REGN9933 *Antibody to Factor XI*	–Thrombosis					
General Medicine						
REGEN-COV (casirivimab and imdevimab)[e][k][l] *Multi-antibody therapy to SARS-CoV-2 virus*			–COVID-19 treatment in hospitalized patients –COVID-19 prevention	–COVID-19 treatment and prevention (U.S.) –EUA amendment to add COVID-19 treatment for hospitalized patients and pre-exposure prophylaxis	–Reported that Phase 3 trials in non-hospitalized COVID-19 patients met primary and key secondary endpoints –Reported that Phase 3 trial in hospitalized COVID-19 patients met its primary endpoint –Positive results reported from Phase 3 RECOVERY trial in hospitalized patients –Reported that all tested doses in Phase 2 dose-ranging study in non-hospitalized patients met its primary endpoint –FDA updated EUA, lowering dose to 1,200 mg, allowing for subcutaneous injections in certain circumstances, and to include post-exposure prophylaxis –FDA revised EUA to exclude use in geographic regions where infection or exposure is likely due to a variant that is not susceptible to the treatment	–FDA decision on BLA (target action date of April 13, 2022) for COVID-19 treatment of non-hospitalized patients and prevention –Submit sBLA and Marketing Authorization Application ("MAA") for COVID-19 treatment of hospitalized patients (first half 2022)

Clinical Program *(continued)*	Phase 1	Phase 2	Phase 3	Regulatory Review[h]	2021 and 2022 Events to Date	Select Upcoming Milestones[i]
REGEN-COV (casirivimab and imdevimab)[e][k][l] *(continued)*					–Approved by EC for COVID-19 treatment of non-hospitalized patients and prevention and by Ministry of Health, Labour and Welfare ("MHLW") for COVID-19 treatment in Japan –Reported that Phase 3 prevention trial in uninfected household contacts of SARS-CoV-2 infected individuals met its primary and key secondary endpoints –Reported positive longer-term results from Phase 3 prevention trial	
Praluent (alirocumab) *Antibody to PCSK9*			–HeFH in pediatrics		–Approved by FDA for HoFH	
Fasinumab[j][f] (REGN475) *Antibody to NGF*			–Osteoarthritis pain of the knee or hip[e]			–Continue discussions with regulatory authorities and determine next steps for the program (mid-2022)
Evkeeza (evinacumab)[f][o] *Antibody to ANGPTL3*		–Acute pancreatitis prevention			–Approved by FDA and EC for HoFH –Completed Phase 2 study in severe hypertriglyceridemia	
Garetosmab[f] (REGN2477) *Antibody to Activin A*		–Fibrodysplasia ossificans progressiva ("FOP")[c][d][e]				–Determine next steps for the program (2022)
REGN4461[f] *Agonist antibody to leptin receptor ("LEPR")*		–Generalized lipodystrophy[e] –Partial lipodystrophy				–Report results from Phase 2 study in generalized lipodystrophy (first half 2022)
REGN5381 *Agonist antibody to NPR1*	–Heart failure					
ALN-HSD[n] *RNAi therapeutic targeting HSD17B13*	–Nonalcoholic steatohepatitis ("NASH")					

Note: For purposes of the table above, a program is classified in Phase 1, 2, or 3 clinical development after recruitment for the corresponding study or studies has commenced

[(a)] In collaboration with Sanofi

[(b)] In collaboration with Bayer outside of the United States

[(c)] FDA granted orphan drug designation

[(d)] FDA granted Breakthrough Therapy designation

[(e)] FDA granted Fast Track designation

[(f)] Sanofi did not opt-in to or elected not to continue to co-develop the product candidate. Under the terms of our agreement, Sanofi is entitled to receive royalties on sales of the product, if any.

[(g)] Studied as monotherapy and in combination with other antibodies and treatments

[(h)] Information in this column relates to U.S., EU, and Japan regulatory submissions only

[(i)] As described in the section preceding the table above and Part I, Item 1A. "Risk Factors," development timelines may be further subject to change as a result of the impact of the COVID-19 pandemic.

[(j)] In collaboration with Teva and Mitsubishi Tanabe Pharma

[(k)] Certain trials conducted with the National Institute of Allergy and Infectious Diseases ("NIAID"), part of the NIH

[(l)] In collaboration with Roche outside of the United States

[(m)] In collaboration with Intellia

[(n)] In collaboration with Alnylam

[(o)] In collaboration with Ultragenyx outside of the United States

Additional Information - Clinical Development Programs

REGEN-COV (casirivimab and imdevimab)

Based on laboratory data that showed markedly decreased binding to the Omicron spike protein, REGEN-COV is highly unlikely to be active against the Omicron variant. In January 2022, the FDA revised the EUA for REGEN-COV to exclude its use in geographic regions where, based on available information including variant susceptibility and regional variant frequency, infection or exposure is likely due to a variant such as Omicron (B.1.1.529) that is not susceptible to the treatment. See "REGEN-COV - Emergency and Temporary Use Authorizations" above for further information.

The Company has completed or discontinued dosing with REGEN-COV in all COVID-19 treatment and prevention studies. However, the Company continues to progress "next generation" antibodies that are active against Omicron, Delta, and other variants of concern. Pending regulatory discussions, new therapeutic candidates could enter clinical development in the coming months.

REGEN-COV Treatment Study - Hospitalized Patients

The Phase 3 UK-based RECOVERY trial in hospitalized patients with severe COVID-19 found that adding REGEN-COV to usual care reduced the risk of death by 20% in patients who had not mounted a natural antibody response on their own against SARS-CoV-2, compared to usual care alone. We were subsequently notified by the sponsor of the RECOVERY trial of a Good Clinical Practices ("GCPs") inspection of the trial by the UK MHRA, which found certain deviations from GCP compliance. The MHRA report stated that it found no evidence that the identified issues had impacted the overall data integrity to such an extent that the data would be unreliable based on those findings. However, it noted that certain aspects of data quality could not be fully assured and requested that certain corrective and preventative actions be taken; the sponsor of the trial has been in discussions with the MHRA and is responding to these findings. We have shared this information with the FDA.

In the Company-sponsored Phase 2/3 study in hospitalized patients, REGEN-COV met the primary virologic endpoint, showing that REGEN-COV reduced viral load in these hospitalized patients, but did not achieve statistical significance in the pre-specified primary clinical endpoint: reduction in mechanical ventilation or death from day 6 to day 29 in patients with high viral load at baseline. However, the study showed a reduction in mechanical ventilation or death from day 1 to day 29 in all patients who were SARS-CoV-2 PCR-positive at baseline. In addition, an approximately 36% reduction in all-cause mortality was seen from day 1 to day 29, supporting the results of the RECOVERY trial.

In September 2021, the Company announced that a Phase 3 trial in patients hospitalized with COVID-19 met its primary endpoint. The trial showed that REGEN-COV significantly reduced viral load within 7 days of treatment in patients who entered the trial without having mounted their own antibody response (seronegative) and required low-flow or no supplemental oxygen. Patients who received REGEN-COV in this trial experienced a 36% reduced risk of death within 29 days of receiving treatment, and in patients who were seronegative when they entered the trial the risk of death was reduced by 56%.

REGEN-COV Prevention Study

In April 2021, we announced positive results from the Phase 3 COVID-19 prevention trial in household contacts of SARS-CoV-2 infected individuals. The trial, which was jointly run with the NIAID, part of the NIH, met its primary and key secondary endpoints, showing that REGEN-COV 1,200 mg subcutaneous injection reduced the risk of symptomatic infections by 81% in those who were not infected.

In November 2021, we announced additional positive results from the Phase 3 COVID-19 prevention trial jointly run with the NIAID, showing the a single dose of REGEN-COV reduced the risk of contracting COVID-19 by 81.6% during the pre-specified follow-up period (months 2–8), maintaining the risk reduction reported during the first month after administration, which is described above.

Descriptions of Marketed Products Studied in Additional Indications and Product Candidates in Late-Stage Clinical Development

EYLEA (aflibercept)

EYLEA (2 mg intravitreal injection) is a soluble fusion protein that acts as a vascular endothelial growth factor ("VEGF") inhibitor, formulated as an injection for the eye. It is designed to block the growth of new blood vessels and decrease the ability of fluid to pass through blood vessels (vascular permeability) in the eye by blocking VEGF-A and PLGF, two growth factors involved in angiogenesis.

Aflibercept 8 mg

Aflibercept 8 mg is an investigational soluble fusion protein that acts as a VEGF inhibitor (see related description under "EYLEA (aflibercept)" above). This concentrated aflibercept formulation is being studied in wet AMD and DME, investigating dosing intervals of every 12 weeks and every 16 weeks.

Dupixent (dupilumab)

Dupixent is a fully human monoclonal antibody that inhibits signaling of the IL-4 and IL-13 pathways, and is not an immunosuppressant. IL-4 and IL-13 are key and central drivers of the type 2 inflammation that plays a major role in atopic dermatitis, asthma, and CRSwNP, and potentially other chronic allergic diseases.

Kevzara (sarilumab)

Kevzara is a fully human monoclonal antibody that binds specifically to the IL-6 receptor and inhibits IL-6-mediated signaling. IL-6 is a signaling protein produced in increased quantities in patients with RA and has been associated with disease activity, joint destruction, and other systemic problems.

Itepekimab

Itepekimab is an investigational, fully human monoclonal antibody that inhibits IL-33, a protein that is believed to play a key role in lung inflammation in COPD.

REGN1908-1909

REGN1908-1909 is an investigational, novel cocktail of two fully human monoclonal immunoglobulin G antibodies that is designed to specifically bind and block the Fel d 1 allergen, thus preventing it from binding and triggering the endogenous antibodies that cause allergies (i.e., immunoglobulin E antibodies). Cat allergy is primarily caused by exposure to Fel d 1, the major allergen in cat dander produced by all cats.

REGN5713-5714-5715

REGN5713-5714-5715 is an investigational combination of three fully human monoclonal antibodies designed to treat allergic inflammatory conditions caused by the allergen Betv1, which is the main allergen responsible for birch pollen allergies. Birch pollen allergy is one of the most common causes of seasonal allergies that occur in the spring, and is also believed to trigger "oral allergy syndrome" food reactions to related allergens found in nuts and fruits such as apples, pears, and cherries.

Libtayo (cemiplimab)

Libtayo is a fully human monoclonal antibody targeting the immune checkpoint receptor PD-1 on T-cells. The PD-1/PD-L1 immune checkpoint pathway is a well-known mechanism by which cancers evade immune destruction. Regeneron is studying Libtayo as monotherapy and in combination with either conventional or novel therapeutic approaches in various solid tumors and blood cancers. It is also being studied in combination with proprietary anti-cancer assets of other companies.

Odronextamab

Odronextamab is an investigational bispecific monoclonal antibody designed to bind to a component of the T-cell receptor ("TCR") complex (CD3), while also binding and bridging T-cells to a protein expressed on B-cells (CD20). We are studying whether odronextamab may help to activate T-cells via their CD3 receptors and trigger targeted, T-cell mediated killing of cancerous cells in several types of B-cell non-Hodgkin lymphoma.

REGN5458

REGN5458 is an investigational bispecific monoclonal antibody designed to bind to CD3 while also binding and bridging T-cells to the BCMA protein on multiple myeloma cells. We are studying whether REGN5458 may help to activate T-cells via their CD3 receptors and trigger targeted, T-cell mediated killing of multiple myeloma.

Pozelimab

Pozelimab is an investigational, fully human monoclonal antibody designed to block complement factor C5 in order to treat diseases mediated by abnormal complement pathway activity, including PNH, CD55-deficient protein-losing enteropathy, and myasthenia gravis. Pozelimab is being studied as monotherapy and also in combination with Alnylam's investigational siRNA therapy, cemdisiran.

REGEN-COV (casirivimab and imdevimab)

REGEN-COV is an investigational cocktail of two fully human monoclonal antibodies designed to prevent and treat infection from the SARS-CoV-2 virus. The two potent, virus-neutralizing antibodies that form the cocktail bind non-competitively to the critical receptor binding domain of the virus's spike protein.

Praluent (alirocumab)

Praluent is a fully human monoclonal antibody that inhibits the binding of PCSK9 to the LDL receptor. Through inhibiting PCSK9, Praluent increases the number of available LDL receptors on the surface of liver cells to clear LDL, which lowers LDL cholesterol levels in the blood.

Fasinumab

Fasinumab is an investigational, fully human monoclonal antibody that targets NGF, a protein that plays a central role in the regulation of pain signaling, and is a potential new way to manage pain without resorting to opioids.

Evkeeza (evinacumab)

Evkeeza is a fully human monoclonal antibody that specifically binds to and blocks ANGPTL3. ANGPTL3 plays a key role in regulating plasma lipid levels, including triglycerides, LDL cholesterol, and HDL cholesterol, through inhibition of lipase enzymes (lipoprotein lipase and endothelial lipase).

Other Programs

Our preclinical research programs include the areas of oncology/immuno-oncology, angiogenesis, ophthalmology, metabolic and related diseases, muscle diseases and disorders, inflammation and immune diseases, bone and cartilage, pain and neurobiology, cardiovascular diseases, infectious diseases, diseases related to aging, and rare diseases.

Research and Development Technologies

Many proteins that play an important role in biology and disease are secreted by cells or located on the cell surface. Moreover, cells communicate through secreted factors and surface molecules. Our scientists have developed two different technologies to make protein therapeutics that potently and specifically block, activate, or inhibit the action of specific cell surface or secreted molecules. The first technology fuses receptor components to the constant region of an antibody molecule to make a class of drugs we call "Traps". EYLEA, ZALTRAP, and ARCALYST are drugs generated using our Trap technology. *VelociSuite*® is our second technology platform, which is used for discovering, developing, and producing fully human antibodies that can address both secreted and cell-surface targets.

VelociSuite

VelociSuite consists of *VelocImmune*®, *VelociGene*®, *VelociMouse*®, *VelociMab*®, *Veloci-Bi*®, *VelociT*®, *VelociHum*®, and other related technologies. The *VelocImmune* mouse platform is utilized to produce fully human antibodies. *VelocImmune* was generated by leveraging our *VelociGene* technology (see below), in a process in which six megabases of mouse immune gene loci were replaced, or "humanized," with corresponding human immune gene loci. *VelocImmune* mice can be used efficiently to generate fully human antibodies to targets of therapeutic interest. *VelocImmune* and our entire *VelociSuite* offer the potential to increase the speed and efficiency through which human antibody therapeutics may be discovered and validated, thereby improving the overall efficiency of our early stage drug development activities. We are utilizing the *VelocImmune* technology to produce our next generation of therapeutic antibody drug candidates for preclinical and clinical development.

Our *VelociGene* platform allows custom and precise manipulation of very large sequences of DNA to produce highly customized alterations of a specified target gene, or genes, and accelerates the production of knock-out and transgenic expression models. In producing knock-out models, a color or fluorescent marker may be substituted in place of the actual gene sequence, allowing for high-resolution visualization of precisely where the gene is active in the body during normal body functioning as well as in disease processes. For the optimization of preclinical development and pharmacology programs, *VelociGene* offers the opportunity to humanize targets by replacing the mouse gene with the human homolog. Thus, *VelociGene* allows scientists to rapidly identify the physical and biological effects of deleting or over-expressing the target gene, as well as to characterize and test potential therapeutic molecules.

Our *VelociMouse* technology platform allows for the direct and immediate generation of genetically altered mice from embryonic stem cells ("ES cells"), thereby avoiding the lengthy process involved in generating and breeding knockout mice from chimeras. Mice generated through this method are normal and healthy and exhibit a 100% germ-line transmission. Furthermore, mice developed using our *VelociMouse* technology are suitable for direct phenotyping or other studies. We have also developed our

VelociMab platform for the rapid screening of antibodies and rapid generation of expression cell lines for our Traps and our *VelocImmune* human antibodies.

We have utilized our *VelociSuite* technologies to develop a class of potential drug candidates, known as bispecific antibodies. *Veloci-Bi* allows for the generation of full-length bispecific antibodies similar to native antibodies that are amenable to production by standard antibody manufacturing techniques, and are likely to have favorable antibody-like pharmacokinetic properties. In the area of immunotherapies in oncology, we are exploring the use of bispecific antibodies that target tumor antigens and the CD3 receptor on T-cells to harness the oncolytic properties of T-cells. We are exploring additional indications and applications for our bispecific technologies, including a new class of CD28 and 4-1BB costimulatory bispecifics.

The *VelociT* mouse extends our research and drug discovery capabilities into cell-mediated immunity and therapeutic TCRs for oncology and other indications. *VelociT* was developed by using our *VelociGene* technology to humanize genes encoding TCRα and TCRβ variable sequences, CD4 and CD8 co-receptors, β2m, and class-I and -II major histocompatibility complexes. As a result, *VelociT* mice generate fully human TCRs, providing for customized modeling of T-cell function in different diseases and a powerful platform for the discovery of unique TCR-based therapies. We are also able to produce antibodies that recognize intracellular peptides bound in the groove of human leukocyte antigen ("HLA"), enabling the targeting of intracellular proteins in cancer cells.

VelociHum is our immunodeficient mouse platform that can be used to accurately test human therapeutics against human immune cells and to study human tumor models. Through genetic humanizations, *VelociHum* mice have been optimized to allow for better development of human immune cells *in vivo*, as well as to allow for engraftment of primary patient-derived tumors that do not take in other commercially available mice.

Regeneron Genetics Center®

Regeneron Genetics Center (RGC™), a wholly owned subsidiary of Regeneron Pharmaceuticals, Inc., leverages de-identified clinical, genomic, and molecular data from human volunteers to identify medically relevant associations in a blinded fashion designed to preserve patients' privacy. The objective of RGC is to expand the use of human genetics for discovering and validating genetic factors that cause or influence a range of diseases where there are major unmet medical needs, with the prospect of improving the drug discovery and development process and to advance innovation in clinical care design. RGC is undertaking multiple collaborative approaches to study design and implementation, including large population-based efforts as well as family- and founder-based approaches. RGC utilizes laboratory automation and innovative approaches to cloud computing to achieve high-quality throughput.

Central to the work of RGC is the portfolio of collaborations with over 100 academic and clinical collaborators around the world, including the University of Colorado, Geisinger Health System, Mayo Clinic, University of Pennsylvania, UCLA Medical Center, UK Biobank, and the University of Helsinki. These collaborations provide access to biological samples and associated phenotype data from consented patient volunteers for purposes of genomic research. RGC undertakes genetic sequencing of these samples to create a unique resource of de-identified genetic data and associated phenotype data for research. Furthermore, the RGC has deployed bulk RNA sequencing, whole genome sequencing, and an O-LINK proteomic assay to complement whole exome sequencing and genotyping. In addition, the RGC leverages organoid models, silencing RNA ("siRNA"), and CRISPR knockout models to validate genetic associations that lead to new therapeutic targets. The RGC continues to publish results from its research efforts in journals and publications in collaboration with its collaborators to advance the field of genomics.

These efforts at the RGC have led to the identification of more than 10 novel genetic targets. Through our Regeneron Genetics Medicines initiative, we are currently advancing these targets using either our *VelociSuite* technologies or other technologies, such as siRNA gene silencing, genome editing, and targeted viral-based gene delivery and expression. See the "Collaboration, License, and Other Agreements" section below for descriptions of our collaborations with Alnylam and Intellia.

Agreements Related to COVID-19

U.S. Government

In the first quarter of 2020, the Company announced an expansion of its Other Transaction Agreement with the Biomedical Advanced Research Development Authority ("BARDA"), pursuant to which the U.S. Department of Health and Human Services ("HHS") was obligated to fund certain of our costs incurred for research and development activities related to COVID-19 treatments.

In July 2020, the Company entered into an agreement with entities acting at the direction of BARDA and the U.S. Department of Defense to manufacture and deliver filled and finished drug product of REGEN-COV to the U.S. government. The agreement, as subsequently amended, provided for payments to the Company of up to $465.9 million in the aggregate for bulk manufacturing of the drug substance, as well as fill/finish, storage, and other activities.

In January 2021, the Company announced an agreement with an entity acting on behalf of the U.S. Department of Defense and HHS to manufacture and deliver additional filled and finished drug product of REGEN-COV to the U.S. government. Pursuant to the agreement, the U.S. government was obligated to purchase 1.25 million doses of drug product, resulting in payments to the Company of $2.625 billion (as described under "Products - REGEN-COV - Emergency and Temporary Use Authorizations" above).

In September 2021, the Company announced an amendment to its January 2021 agreement to supply the U.S. government with an additional 1.4 million doses of REGEN-COV. Pursuant to the agreement, the U.S. government was obligated to purchase all filled and finished doses of such additional drug product delivered by January 31, 2022, resulting in payments to the Company of $2.940 billion in the aggregate. Additionally, Roche supplied a portion of the doses to Regeneron to fulfill our agreement with the U.S. government (see "Roche" section below for further details regarding our collaboration agreement with Roche).

As of December 31, 2021, the Company had completed its final deliveries of drug product under the agreements described above. See "Results of Operations - Revenues" below for REGEN-COV net product sales recognized in connection with these agreements.

Roche

In August 2020, we entered into a collaboration agreement with Roche to develop, manufacture, and distribute the casirivimab and imdevimab antibody cocktail. We lead global development activities for casirivimab and imdevimab, and the parties jointly fund certain ongoing studies, as well as any mutually agreed additional new global studies to evaluate further the potential of casirivimab and imdevimab in treating or preventing COVID-19.

Under the terms of the agreement, each party is obligated to dedicate a certain amount of manufacturing capacity to casirivimab and imdevimab each year. We distribute the product in the United States and Roche distributes the product outside of the United States. The parties share gross profits from worldwide sales based on a pre-specified formula, depending on the amount of manufactured product supplied by each party to the market.

Collaboration, License, and Other Agreements

Sanofi

Antibody

We are collaborating with Sanofi on the global development and commercialization of Dupixent, Kevzara, and itepekimab (the "Antibody Collaboration"). Under the terms of the Antibody License and Collaboration Agreement (the "LCA"), Sanofi is generally responsible for funding 80%–100% of agreed-upon development costs. We are obligated to reimburse Sanofi for 30%–50% of worldwide development expenses that were funded by Sanofi based on our share of collaboration profits from commercialization of collaboration products. However, we are only required to apply 10% of our share of the profits from the Antibody Collaboration in any calendar quarter to reimburse Sanofi for these development costs.

Under our collaboration agreement, Sanofi records product sales for commercialized products, and Regeneron has the right to co-commercialize such products on a country-by-country basis. We co-commercialize Dupixent in the United States and in certain countries outside the United States. We supply certain commercial bulk product to Sanofi. We and Sanofi equally share profits and losses from sales within the United States. We and Sanofi share profits outside the United States on a sliding scale based on sales starting at 65% (Sanofi)/35% (us) and ending at 55% (Sanofi)/45% (us), and share losses outside the United States at 55% (Sanofi)/45% (us). In addition to profit and loss sharing, we are entitled to receive sales milestone payments from Sanofi. In each of 2020 and 2021, the Company earned a $50.0 million sales-based milestone from Sanofi, upon aggregate annual sales of antibodies outside the United States (including Praluent) exceeding $1.0 billion and $1.5 billion, respectively, on a rolling twelve-

month basis. We are entitled to receive up to an aggregate of $150.0 million in additional sales milestone payments from Sanofi, which includes the next sales milestone payment of $50.0 million that would be earned when such sales outside the United States exceed $2.0 billion on a rolling twelve-month basis.

In April 2020, the Company and Sanofi entered into an amendment to the LCA in connection with, among other things, the removal of Praluent from the LCA such that (i) effective April 1, 2020, the LCA no longer governs the development, manufacture, or commercialization of Praluent and (ii) the quarterly period ended March 31, 2020 was the last quarter for which Sanofi and the Company shared profits and losses for Praluent under the LCA. The parties also entered into a Praluent Cross License & Commercialization Agreement (the "Praluent Agreement") pursuant to which, effective April 1, 2020, the Company, at its sole cost, became solely responsible for the development and commercialization of Praluent in the United States, and Sanofi, at its sole cost, is solely responsible for the development and commercialization of Praluent outside of the United States. Under the Praluent Agreement, Sanofi will pay the Company a 5% royalty on Sanofi's net product sales of Praluent outside the United States until March 31, 2032. The Company will not owe Sanofi royalties on the Company's net product sales of Praluent in the United States. Although each party will be responsible for manufacturing Praluent for its respective territory, the parties have entered into definitive supply agreements under which, for a certain transitional period, the Company will continue to supply drug substance to Sanofi and Sanofi will continue to supply finished product to Regeneron. With respect to any intellectual property or product liability litigation relating to Praluent, the parties have agreed that, effective April 1, 2020, Regeneron and Sanofi each will be solely responsible for any such litigation (including damages and other costs and expenses thereof) in the United States and outside the United States, respectively, arising out of Praluent sales or other activities on or after April 1, 2020 (subject to Sanofi's right to set off a portion of any third-party royalty payments resulting from certain patent litigation proceedings against up to 50% of any Praluent royalty payment owed to Regeneron). The parties will each bear 50% of any damages arising out of Praluent sales or other activities prior to April 1, 2020.

Immuno-Oncology

We are collaborating with Sanofi on the development and commercialization of antibody-based cancer treatments in the field of immuno-oncology (the "IO Collaboration").

Effective December 31, 2018, the Company and Sanofi entered into an Amended and Restated Immuno-oncology Discovery and Development Agreement (the "Amended IO Discovery Agreement"), which narrowed the scope of the existing discovery and development activities conducted by the Company ("IO Development Activities") under the original 2015 Immuno-oncology Discovery and Development Agreement (the "2015 IO Discovery Agreement") to developing therapeutic bispecific antibodies targeting (i) BCMA and CD3 (the "BCMAxCD3 Program") and (ii) MUC16 and CD3 (the "MUC16xCD3 Program") through clinical proof-of-concept. The Amended IO Discovery Agreement provided for, among other things, Sanofi's prepayment for certain IO Development Activities regarding the BCMAxCD3 Program and the MUC16xCD3 Program. Under the terms of the Amended IO Discovery Agreement, the Company was required to conduct development activities with respect to (i) the BCMAxCD3 Program through the earlier of clinical proof-of-concept or the expenditure of $70.0 million (the "BCMAxCD3 Program Costs Cap") and (ii) the MUC16xCD3 Program through the earlier of clinical proof-of-concept or the expenditure of $50.0 million (the "MUC16xCD3 Program Costs Cap"). We are obligated to reimburse Sanofi for half of the development costs they funded that are attributable to clinical development of antibody product candidates under the Amended IO Discovery Agreement from our share of profits from commercialized IO Collaboration products.

With regard to the BCMAxCD3 Program and the MUC16xCD3 Program, when the applicable Program Costs Cap was reached, Sanofi had the option to license rights to the product candidate and other antibodies targeting the same targets for, with regard to BCMAxCD3, immuno-oncology indications, and with regard to MUC16xCD3, all indications, pursuant to the Immuno-oncology License and Collaboration Agreement (the "IO License and Collaboration Agreement"), as amended. During the first quarter of 2021, Sanofi did not exercise its options to license rights to these product candidates; as a result, we retain the exclusive right to develop and commercialize such product candidates and Sanofi will receive a royalty on sales (if any).

Under the terms of the IO License and Collaboration Agreement, the parties are co-developing and co-commercializing Libtayo. We have principal control over the development of Libtayo, and the parties share equally, on an ongoing basis, development and commercialization expenses for Libtayo. With regard to Libtayo, we lead commercialization activities in the United States, while Sanofi leads commercialization activities outside of the United States and the parties equally share profits from worldwide sales. Sanofi has exercised its option to co-commercialize Libtayo in the United States. We will be entitled to a milestone payment of $375.0 million in the event that global sales of Libtayo equal or exceed $2.0 billion in any consecutive twelve-month period.

Bayer

EYLEA and aflibercept 8 mg outside the United States

We and Bayer are parties to a license and collaboration agreement for the global development and commercialization of EYLEA and aflibercept 8 mg outside the United States. All agreed-upon development expenses incurred by the Company and Bayer are shared equally. Bayer markets EYLEA outside the United States, where, for countries other than Japan, the companies share equally in profits and losses from sales. In Japan, we were entitled to receive a tiered percentage of between 33.5% and 40.0% of EYLEA net sales through 2021, and thereafter, the companies share equally in profits and losses from sales.

We are obligated to reimburse Bayer for 50% of the development costs that it has incurred under the agreement from our share of the collaboration profits (including payments to us based on sales in Japan). The reimbursement payment in any quarter will equal 5% of the then outstanding repayment obligation, but never more than our share of the collaboration profits in the quarter unless we elect to reimburse Bayer at a faster rate.

Within the United States, we retain exclusive commercialization rights and are entitled to all profits from such sales.

Teva

Fasinumab

We and Teva are parties to a collaboration agreement to develop and commercialize fasinumab globally, excluding certain Asian countries that are subject to our collaboration agreement with Mitsubishi Tanabe Pharma Corporation ("MTPC"). In connection with the agreement, Teva made a $250.0 million non-refundable up-front payment. We lead global development activities, and the parties share equally, on an ongoing basis, development costs under a global development plan. As of December 31, 2021, we had received an aggregate $120.0 million of development milestones from Teva, and we are entitled to receive up to an aggregate of $340.0 million in additional development milestones and up to an aggregate of $1.890 billion in contingent payments upon achievement of specified annual net sales amounts. We are responsible for the manufacture and supply of fasinumab globally.

Within the United States, we will lead commercialization activities, and the parties will share equally in any profits or losses in connection with commercialization of fasinumab. In the territory outside of the United States, Teva will lead commercialization activities and we will supply product to Teva at a tiered purchase price, which is calculated as a percentage of net sales of the product (subject to adjustment in certain circumstances).

Zai Lab

Odronextamab (REGN1979)

In 2020, we entered into an agreement with Zai Lab Limited to develop and commercialize odronextamab in mainland China, Hong Kong, Taiwan, and Macau (the "Zai Territories"). In connection with the agreement, Zai made a $30.0 million non-refundable up-front payment to the Company. We continue to lead global development activities for odronextamab, and Zai is responsible for funding a portion of the global development costs for certain clinical trials.

We are responsible for the manufacture and supply of clinical and commercial product of odronextamab to Zai. If odronextamab is commercialized in the Zai Territories, we will supply the product to Zai at a tiered purchase price, which is calculated as a percentage of net sales of the product (subject to adjustment in certain circumstances), and we are eligible to receive up to $160.0 million in additional regulatory and sales milestone payments.

Alnylam

In 2018, we and Alnylam Pharmaceuticals, Inc. entered into a collaboration to discover RNA interference ("RNAi") therapeutics for NASH and potentially other related diseases, as well as to research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts (including ALN-HSD, which is currently in clinical development). ALN-HSD is being co-developed with Alnylam with terms generally consistent with the form of a Co-Commercialization Collaboration Agreement in connection with the 2019 collaboration agreement as described below. Alnylam is conducting the Phase 1 clinical trial for ALN-HSD and Regeneron will be the lead party for all future development.

In 2019, we and Alnylam entered into a global, strategic collaboration to discover, develop, and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic disease targets expressed in the eye and central nervous system ("CNS"), in addition to a select number of targets expressed in the liver. Under the terms of the agreement, we made an up-front payment of $400.0 million to Alnylam. For each program, we will provide Alnylam with a specified amount of funding at program initiation and at lead candidate designation, and Alnylam is eligible to receive up to an aggregate of $200.0 million in clinical proof-of-principle milestones for eye and CNS programs.

Under the collaboration, the parties plan to perform discovery research until designation of lead candidates. Following designation of a lead candidate, the parties may further advance such lead candidate under either a License Agreement or a Co-Commercialization Collaboration Agreement structure. The initial target nomination and discovery period is five years (which may under certain situations automatically be extended for up to seven years in the aggregate) (the "Research Term"). In addition, we have an option to extend the Research Term for an additional five-year period for a research extension fee ranging from $200.0 million to $400.0 million; the actual amount of the fee will be determined based on the acceptance of one or more Investigational New Drug Applications ("INDs") (or their equivalent in certain other countries) for programs in the eye and CNS.

At the stage of designation of a lead candidate for CNS programs and liver programs, the parties have alternating rights to be a lead party for collaboration products. At the stage of designation of a lead candidate for eye programs, we have the sole right to take the product forward as a licensee. The lead party is required to take the program forward under the License Agreement structure unless the other party exercises its rights to opt-in to a Co-Commercialization Collaboration Agreement, in which case the lead party is required to take the program forward under the Co-Commercialization Collaboration Agreement structure. Alnylam does not have rights to opt-in to a Co-Commercialization Collaboration Agreement for eye programs.

Under a License Agreement, the lead party is designated as the licensee and has the right to develop and commercialize the collaboration product under such program. The licensee will be responsible for its own costs and expenses incurred in connection with the development and commercialization of the collaboration products under the License Agreement. The licensee will pay to the licensor certain development and/or commercialization milestone payments, as well as certain tiered royalty payments to the licensor based on the aggregate annual net sales of the collaboration product.

For CNS programs and liver programs, as soon as a party is designated as a lead party, the other company has rights to opt-in to a Co-Commercialization Collaboration Agreement as a participating party. Under a Co-Commercialization Collaboration Agreement, the party designated as the lead party will lead development and commercialization of the program and the parties will split profits and share costs equally, subject to certain co-funding opt-outs at specified clinical trial phases or under other conditions. If a party exercises its co-funding opt-out right, the lead party will be required to make certain tiered royalty payments to the other party based on the aggregate annual net sales of the collaboration product and the timing of the exercise of the co-funding opt-out right. If the non-lead party does not initially opt-in to a Co-Commercialization Collaboration Agreement, the lead party has the right to take the program forward under a License Agreement structure.

Under the collaboration, when we are the licensee under a License Agreement or the lead party under a Co-Commercialization Collaboration Agreement, Alnylam will be responsible for the manufacture and supply of the product to us for Phase 1 and Phase 2 clinical trials.

In connection with the collaboration, we also purchased shares of Alnylam common stock for aggregate cash consideration of $400.0 million.

In 2019, the parties entered into a Co-Commercialization Collaboration Agreement for an siRNA therapeutic targeting the C5 component of the human complement pathway being developed by Alnylam, with Alnylam as the lead party, and a License Agreement for a combination product consisting of cemdisiran and pozelimab, with us as the licensee. Under the C5 siRNA Co-Commercialization Collaboration agreement, the parties share costs equally and will split profits (if commercialized); and under the License Agreement, the licensee is responsible for its own costs and expenses. The C5 siRNA License Agreement contains a flat low double-digit royalty payable to Alnylam on our potential future net sales of the combination product only subject to customary reductions, as well as up to $325.0 million in sales milestones.

Intellia

In 2016, we entered into a license and collaboration agreement with Intellia Therapeutics, Inc. to advance CRISPR/Cas9 gene-editing technology for *in vivo* therapeutic development. NTLA-2001, which is in clinical development, is subject to a co-development and co-commercialization arrangement pursuant to which Intellia will lead development and commercialization activities and the parties share an agreed-upon percentage of development expenses and profits (if commercialized).

In May 2020, we expanded our existing collaboration with Intellia Therapeutics, Inc. to provide us with rights to develop products for additional *in vivo* CRISPR/Cas9-based therapeutic targets and for the companies to jointly develop potential products for the treatment of hemophilia A and B, with Regeneron leading development and commercialization activities. In addition, we also received non-exclusive rights to independently develop and commercialize *ex vivo* gene edited products. In connection with the May 2020 agreement, we made a $70.0 million up-front payment and purchased shares of Intellia common stock for an aggregate purchase price of $30.0 million.

BARDA

We and BARDA are parties to agreements pursuant to which HHS provided certain funding to develop, test, and manufacture a treatment for Ebola virus infection. In July 2020, HHS exercised its option under an existing agreement to provide up to $344.6 million of additional funding for the manufacture and supply of Inmazeb. We expect to deliver a pre-specified number of Inmazeb treatment doses over the course of approximately six years.

See "Agreements Related to COVID-19 - U.S. Government" section above for information related to our COVID-19 agreements.

Kiniksa

ARCALYST

As described under "Products" above, pursuant to a 2017 license agreement, we granted Kiniksa Pharmaceuticals, Ltd. the right to develop and commercialize certain new indications for ARCALYST. During the first quarter of 2021, Kiniksa received marketing approval in the United States for a new indication of ARCALYST, recurrent pericarditis, and, as a result, we received a $20.0 million milestone payment from Kiniksa. The quarterly period ended March 31, 2021 was the last quarter for which the Company recorded net product sales of ARCALYST.

Following this approval, Kiniksa is solely responsible for the U.S. development and commercialization of ARCALYST in all approved indications, and Regeneron will continue to supply clinical and commercial product to Kiniksa. Kiniksa will pay Regeneron 50% of its profits from sales of ARCALYST and the parties will not share in any losses incurred by Kiniksa in connection with commercialization of ARCALYST.

Ultragenyx

As described under "Products" above, in January 2022 we entered into a license and collaboration agreement for Ultragenyx Pharmaceutical Inc. to develop and commercialize Evkeeza in countries outside of the United States. In connection with the agreement, Ultragenyx made a $30.0 million non-refundable up-front payment to the Company. Ultragenyx will share in certain costs for global trials led by the Company and also have the right to continue to clinically develop Evkeeza in countries outside of the U.S. We will supply commercial product to Ultragenyx at a tiered purchase price, which is calculated as a percentage of net sales of the product (subject to adjustment in certain circumstances), and are eligible to receive additional regulatory and sales milestone payments.

We have also granted Ultragenyx an exclusive option to negotiate a separate agreement to collaborate on the development and commercialization of garetosmab outside of the United States under terms to be agreed upon by both companies.

Manufacturing

We currently manufacture bulk drug materials and products at our manufacturing facilities in Rensselaer, New York and Limerick, Ireland. These facilities consist of owned and leased research, manufacturing, office, laboratory, and warehouse space. In addition, during 2022, we expect to continue the construction of a fill/finish facility in Rensselaer, New York.

We currently have approximately 100,000 liters of cell culture capacity at our Rensselaer facility, and are approved by the FDA and other regulatory agencies to manufacture our bulk drug materials and products. In addition, we currently have approximately 130,000 liters of cell culture capacity at our Limerick facility which has received certain manufacturing approvals by regulatory agencies, including the FDA.

Certain bulk drug materials and products are also manufactured by our collaborators, and certain raw materials or products necessary for the manufacture and formulation of our products and product candidates are provided by single-source unaffiliated third-party suppliers. In addition, we rely on our collaborators or third parties to perform packaging, filling, finishing, labeling, distribution, laboratory testing, and other services related to the manufacture of our products and product candidates, and to supply various raw materials and other products. See Part I, Item 1A. "Risk Factors - Risks Related to Manufacturing and Supply" for further information.

Among the conditions for regulatory marketing approval of a medicine is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the good manufacturing practice ("GMP") regulations of the health authority. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, are also subject to inspections by or under the authority of the FDA and by other national, federal, state, and local agencies.

Commercial

Our medicines are marketed through our commercial group, which includes experienced professionals in the fields of marketing, professional education, patient education, reimbursement and market access, trade and distribution, commercial operations, commercial analytics, market research, and forecasting.

We sell our marketed products in the United States primarily to wholesalers and specialty distributors that serve pharmacies, hospitals, government agencies, physicians, and other healthcare providers. We had sales to two customers (Besse Medical, a subsidiary of AmerisourceBergen Corporation, and McKesson Corporation) that each accounted for more than 10% of total gross product revenue for the year ended December 31, 2021. On a combined basis, our product sales to these customers accounted for 48% of our total gross product revenue for the year ended December 31, 2021. We promote approved medicines to healthcare professionals via our team of U.S.-based field employees, as well as medical journals, medical exhibitions, distribution of literature and samples, and online channels. In addition, we advertise certain products directly to U.S. consumers and maintain websites with information about our medicines. The commercial group also evaluates opportunities for our targets and product candidates and prepares for market launches of new medicines.

Additionally, we are a party to several collaboration agreements, whereby our collaborator is responsible for recording product sales of certain products either solely outside the United States or globally. We have exercised our option to co-commercialize some products in accordance with such collaboration agreements. Refer to "Collaboration, License, and Other Agreements" section above for additional information.

Competition

We face substantial competition from pharmaceutical, biotechnology, and chemical companies. Our ability to compete depends, to a great extent, on how fast we can develop safe and effective product candidates, complete clinical testing and approval processes, and supply commercial quantities of the product to the market. Competition among products approved for sale is based on efficacy, safety, reliability, availability, price, patent position, and other factors.

Marketed Products

The table below provides an overview of the current competitive landscape for the key products marketed by us and/or our collaborators under our collaboration agreements with them in such products' currently approved indications. The table below is provided for illustrative purposes only and is not exhaustive. For additional information regarding the substantial competition these marketed products face, including potential future competition from product candidates in clinical development, see also Part I, Item 1A. "Risk Factors - Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *The commercial success of our products and product candidates is subject to significant competition.*"

Marketed Product	Competitor Product	Competitor	Indication	Territory[(1)]
EYLEA	Lucentis® (ranibizumab injection)	Novartis AG and Genentech/Roche	Wet AMD, DME, macular edema following RVO (including CRVO and BRVO), diabetic retinopathy, mCNV, and ROP	Worldwide
	Byooviz™ (ranibizumab-nuna) (biosimilar referencing Lucentis)	Samsung Bioepis Co., Ltd./Biogen Inc.	Wet AMD, DME, macular edema following RVO (including CRVO and BRVO), diabetic retinopathy, and mCNV	United States, EU
	Susvimo® (ranibizumab ocular implant)	Genentech/Roche	Wet AMD	United States
	Vabysmo™ (faricimab-svoa)	Genentech/Roche	Wet AMD, DME	United States
	Avastin® (bevacizumab) (off-label and repackaged)	Genentech/Roche	Wet AMD, DME, and macular edema following RVO	Worldwide

Marketed Product *(continued)*	Competitor Product	Competitor	Indication	Territory[1]
EYLEA *(continued)*	Beovu® (brolucizumab) Injection	Novartis	Wet AMD	Worldwide
	Ozurdex® (dexamethasone intravitreal implant)	Allergan/AbbVie Inc.	DME, RVO	United States, EU
	Iluvien® (fluocinolone acetonide intravitreal implant)	Alimera Sciences, Inc.	DME	United States, EU
	Conbercept	Chengdu Kanghong Pharmaceutical Group Co., Ltd.	Wet AMD, DME, mCNV	China
Dupixent	Eucrisa®/Staquis® (crisaborole)	Pfizer Inc.	Mild-to-moderate atopic dermatitis	United States, EU
	Olumiant® (baricitinib)	Eli Lilly and Company/ Incyte Corporation	Moderate-to-severe atopic dermatitis	EU, Japan
	Cibinqo® (abrocitinib)	Pfizer	Moderate-to-severe atopic dermatitis	Worldwide
	Rinvoq® (upadacitinib)	AbbVie	Moderate-to-severe atopic dermatitis	Worldwide
	Adbry™/Adtralza® (tralokinumab)	LEO Pharma Inc.	Moderate-to-severe atopic dermatitis	United States, EU
	Corectim® (delgocitinib)	Japan Tobacco Inc./Torii Pharmaceutical Co., Ltd.	Atopic dermatitis	Japan
	Xolair® (omalizumab)	Roche/Novartis	Asthma, nasal polyps	Worldwide (asthma); United States, EU (nasal polyps)
	Nucala® (mepolizumab)	GlaxoSmithKline ("GSK")	Asthma, nasal polyps	Worldwide (asthma); United States, EU (nasal polyps)
	Cinqair® (reslizumab)	Teva	Asthma	United States, EU
	Fasenra® (benralizumab)	AstraZeneca	Asthma	Worldwide
	Tezspire™ (tezepelumab-ekko)	AstraZeneca/Amgen	Asthma	United States
Libtayo	Keytruda® (pembrolizumab)	Merck & Co., Inc.	Various cancers	Worldwide
	Opdivo® (nivolumab)	Bristol-Myers Squibb	Various cancers	Worldwide
	Tecentriq® (atezolizumab)	Roche	Various cancers	Worldwide
	Imfinzi® (durvalumab)	AstraZeneca	Various cancers	Worldwide
	Bavencio® (avelumab)	Pfizer/Merck KGaA	Various cancers	Worldwide
	Jemperli® (dostarlimab)	GSK	Various cancers	United States, EU
Praluent	Repatha® (evolocumab)	Amgen	(1) Reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease, (2) primary hyperlipidemia, and (3) HoFH	Worldwide

Marketed Product *(continued)*	Competitor Product	Competitor	Indication	Territory[(1)]
Praluent *(continued)*	Leqvio® (inclisiran)	Novartis	Primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidemia	United States, EU
Kevzara	Actemra® (tocilizumab)	Genentech/Roche/Chugai Pharmaceutical Co., Ltd.	Rheumatoid arthritis	Worldwide
	Orencia® (abatacept)	Bristol-Myers Squibb	Rheumatoid arthritis	Worldwide
	Xeljanz® (tofacitinib)	Pfizer	Rheumatoid arthritis	Worldwide
	Olumiant® (baricitinib)	Eli Lilly/Incyte	Rheumatoid arthritis	Worldwide
	Rinvoq® (upadacitinib)	AbbVie	Rheumatoid arthritis	Worldwide
	Jyseleca® (filgotinib)	Gilead Sciences, Inc./ Galapagos NV	Rheumatoid arthritis	EU, Japan

[(1)] This table focuses primarily on the United States, EU, and Japan. "Worldwide" indicates that the relevant product is approved in the United States, EU, Japan, and at least one other country.

Product Candidates

Our late-stage and earlier-stage clinical candidates (including those being developed in collaboration with our collaborators) face competition from many pharmaceutical and biotechnology companies. For example, we are aware of other pharmaceutical and biotechnology companies actively engaged in the research and development of antibody-based products against targets that are also the targets of our early- and late-stage product candidates. These companies are using various technologies in competition with our *VelocImmune* technology and our other antibody generation technologies, including their own antibody generation technologies and other approaches such as RNAi, chimeric antigen receptor T cell (CAR-T cell), and gene therapy technologies. We are also aware of several companies developing or marketing small molecules that may compete with our antibody product candidates in various indications, if such product candidates obtain regulatory approval in those indications.

For additional information regarding our product candidates (including those being developed in collaboration with our collaborators) and the substantial competition they face, see also Part I, Item 1A. "Risk Factors - Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *The commercial success of our products and product candidates is subject to significant competition*."

Other Areas

Many pharmaceutical and biotechnology companies are attempting to discover new therapeutics for indications in which we invest substantial time and resources. In these and related areas, intellectual property rights have been sought and certain rights have been granted to competitors and potential competitors of ours, and we may be at a substantial competitive disadvantage in such areas as a result of, among other things, our inferior intellectual property position or lack of experience, trained personnel, and expertise. A number of corporate and academic competitors are involved in the discovery and development of novel therapeutics that are the focus of other research or development programs we are now conducting. Some of these competitors are currently conducting advanced preclinical and clinical research programs in these areas. These and other competitors also may have established substantial intellectual property and other competitive advantages.

If any of these or other competitors announces a successful clinical study involving a product that may be competitive with one of our product candidates or the grant of marketing approval by a regulatory agency for a competitive product, such developments may have an adverse effect on our business, operating results, financial condition, cash flows, or future prospects.

We also compete with academic institutions, governmental agencies, and other public or private research organizations, which conduct research, seek patent and other intellectual property protection, and establish collaborative arrangements for the development and marketing of products that would provide royalties or other consideration for use of their technology. These institutions are becoming more active in seeking patent and other intellectual property protection and licensing arrangements to collect royalties or other consideration for use of the technology they have developed. Products developed in this manner may compete directly with products we develop. We also compete with others in acquiring technology from these institutions, agencies, and organizations.

Patents, Trademarks, and Trade Secrets

We rely on a combination of intellectual property laws, including patent, trademark, copyright, trade secret, and domain name protection laws, as well as confidentiality and license agreements, to protect our intellectual property and proprietary rights.

Our success depends, in part, on our ability to obtain patents, maintain trade secret protection, and operate without infringing on the proprietary rights of third parties (see Part I, Item 1A. "Risk Factors - Risks Related to Intellectual Property and Market Exclusivity - *We may be restricted in our development, manufacturing, and/or commercialization activities by patents or other proprietary rights of others, and could be subject to awards of damages if we are found to have infringed such patents or rights*"; and Note 15 to our Consolidated Financial Statements). Our policy is to file patent applications to protect technology, inventions, and improvements that we consider important to our business and operations. We hold an ownership interest in a number of issued patents in the United States and foreign countries with respect to our products and technologies. In addition, we hold an ownership interest in thousands of patent applications in the United States and foreign countries.

Our patent portfolio includes granted patents and pending patent applications covering our *VelociSuite* technologies, including our *VelocImmune* mouse platform which produces fully human antibodies. Our issued patents covering these technologies generally expire between 2022 and 2032. However, we continue to file patent applications directed to improvements to these technology platforms.

Our patent portfolio also includes issued patents and pending applications relating to commercialized products and our product candidates in clinical development. These patents cover the proteins and DNA encoding the proteins, manufacturing patents, method of use patents, and pharmaceutical compositions.

The following table describes our U.S. patents, European patents ("EP"), and Japanese patents ("JP") that are of particular relevance to key products marketed or otherwise commercialized by us and/or our collaborators, including the territory, patent number, general subject matter class, and expected expiration dates. The noted expiration dates include any patent term adjustments. Certain of these patents may also be entitled to term extensions. We continue to pursue additional patents and patent term extensions in the United States and other jurisdictions covering various aspects of our products that may, if issued, extend exclusivity beyond the expiration of the patents listed in the table below. One or more patents with the same or earlier expiry date may fall under the same "general subject matter class" for certain products and may not be separately listed.

Product	Molecule	Territory	Patent No.	General Subject Matter Class	Expiration
EYLEA[a]	aflibercept	US	7,070,959	Composition of Matter	June 16, 2023[b]
		US	8,092,803	Formulation	June 21, 2027
		US	10,464,992	Formulation	June 14, 2027
		US	10,857,231	Formulation	March 22, 2026
		US	11,066,458	Formulation	June 14, 2027
		US	11,084,865	Formulation	June 14, 2027
		US	9,254,338	Methods of Treatment	May 22, 2032
		US	10,857,205	Methods of Treatment	January 11, 2032
		US	10,828,345	Methods of Treatment	January 11, 2032
		US	10,888,601	Methods of Treatment	January 11, 2032
		US	10,406,226	Method of Manufacturing	March 22, 2026
		EP	1183353	Composition of Matter (Supplementary Protection Certificate)	(May 23, 2025)[c]
		EP	2364691	Formulation	June 14, 2027
		EP	2944306	Formulation	June 14, 2027
		JP	4,723,140	Composition of Matter	December 29, 2022 – December 25, 2023[d]
		JP	5,273,746	Methods of Treatment	June 24, 2022
		JP	5,216,002	Formulation	February 27, 2028 – October 1, 2029[d]
Dupixent[a]	dupilumab	US	7,608,693	Composition of Matter	March 28, 2031[e]
		US	8,945,559	Formulation	October 17, 2032

Product *(continued)*	Molecule	Territory	Patent No.	General Subject Matter Class	Expiration
Dupixent[a] *(continued)*		US	10,435,473	Formulation	October 5, 2031
		US	11,059,896	Formulation	October 5, 2031
		US	8,075,887	Methods of Treatment	April 17, 2028
		US	8,337,839	Methods of Treatment	October 2, 2027
		US	9,290,574	Methods of Treatment	July 10, 2034
		US	9,574,004	Methods of Treatment	December 22, 2033
		US	10,485,844	Methods of Treatment	September 21, 2037
		US	10,059,771	Methods of Treatment	June 20, 2034
		US	11,167,004	Methods of Treatment	September 21, 2037
		US	11,034,768	Methods of Treatment	March 23, 2039
		EP	2356151	Composition of Matter	October 27, 2029[c]
		EP	2356151	(Supplementary Protection Certificate)	(September 28, 2032)[c]
		EP	3010539	Methods of Treatment	June 20, 2034
		EP	2888281	Methods of Treatment	August 20, 2033
		EP	3064511	Methods of Treatment	October 27, 2029
		EP	3107575	Methods of Treatment	February 20, 2035
		EP	3470432	Methods of Treatment	August 20, 2033
		EP	2624865	Formulation	October 5, 2031
		EP	3354280	Formulation	October 5, 2031
		JP	5,291,802	Composition of Matter	October 27, 2029 – October 27, 2034[d]
		JP	5,918,246	Formulation	October 5, 2031 – September 15, 2034[d]
		JP	6,306,588	Methods of Treatment	August 20, 2033 – August 29, 2034[d]
		JP	6,353,838	Methods of Treatment	September 4, 2033
		JP	6,673,840	Methods of Treatment	February 20, 2035
		JP	6,463,351	Methods of Treatment	June 20, 2034
		JP	6,861,630	Methods of Treatment	November 13, 2035
Libtayo	cemiplimab	US	9,987,500	Composition of Matter	September 18, 2035
		US	10,737,113	Composition of Matter	April 10, 2035
		US	10,457,725	Methods of Treatment	May 12, 2037
		EP	3097119	Composition of Matter	January 23, 2035
		EP	3455258	Methods of Treatment	May 12, 2037
		JP	6,425,730	Composition of Matter	January 23, 2035
Praluent[a][f]	alirocumab	US	8,062,640	Composition of Matter	December 15, 2029
		US	10,023,654	Composition of Matter	December 15, 2029
		US	10,472,425	Formulation	July 27, 2032
		US	8,357,371	Methods of Treatment	December 21, 2029
		US	9,550,837	Methods of Treatment	December 15, 2029
		US	9,724,411	Methods of Treatment	January 15, 2031
		US	10,428,157	Methods of Treatment	December 26, 2037
		US	10,544,232	Methods of Treatment	March 13, 2035
		US	10,995,150	Methods of Treatment	June 6, 2034
		US	11,116,839	Methods of Treatment	June 14, 2033
		EP	2358756	Composition of Matter	December 15, 2029[c]

Product *(continued)*	Molecule	Territory	Patent No.	General Subject Matter Class	Expiration
Praluent[a][f] *(continued)*		EP	2358756	(Supplementary Protection Certificate)	(September 25, 2030)[c]
		EP	3156422	Composition of Matter	December 15, 2029
		EP	2756004	Methods of Treatment	September 12, 2032
		EP	3055333	Methods of Treatment	October 10, 2034
		EP	3169353	Methods of Treatment	July 16, 2035
		EP	3169362	Methods of Treatment	July 16, 2035
		EP	3004171	Methods of Treatment	June 6, 2034
		EP	3068803	Methods of Treatment	November 12, 2034
		EP	3395836	Methods of Manufacturing	January 27, 2032
Kevzara	sarilumab	US	7,582,298	Composition of Matter	May 22, 2031[g]
		US	10,072,086	Formulation	September 19, 2031
		US	11,098,127	Formulation	January 7, 2031
		US	8,080,248	Methods of Treatment	June 1, 2027
		US	8,568,721	Methods of Treatment	June 1, 2027
		US	9,943,594	Methods of Treatment	December 28, 2033
		US	10,927,435	Methods of Treatment	October 10, 2032
		EP	2041177	Composition of Matter	June 1, 2027[c]
		EP	2041177	(Supplementary Protection Certificate)	(June 1, 2032)[c]
		EP	2766039	Methods of Treatment	October 10, 2032
		EP	3071230	Methods of Treatment	November 21, 2034
		EP	3409269	Formulation	January 7, 2031
		JP	5,307,708	Composition of Matter	June 1, 2027 – August 22, 2031[d]
		JP	5,805,660	Formulation	January 7, 2031 – October 24, 2031[d]
		JP	6,122,018	Methods of Treatment	October 10, 2032 – March 29, 2033[d]
		JP	6,657,089	Methods of Treatment	November 21, 2034
REGEN-COV[a]	casirivimab and imdevimab	US	10,787,501	Composition of Matter	June 25, 2040
		US	10,975,139	Composition of Matter	June 25, 2040

[a] See Note 15 to our Consolidated Financial Statements for information regarding *inter partes* review and post-grant review petitions filed in the U.S. Patent and Trademark Office relating to EYLEA and patent infringement proceedings relating to Dupixent, Praluent, and REGEN-COV.

[b] A patent term extension has been granted by the U.S. Patent and Trademark Office, extending the original patent term (May 23, 2020), insofar as it covers EYLEA, to June 16, 2023.

[c] Supplementary protection certificates ("SPCs") are pending and/or have been granted in various European countries, extending the original patent terms in those countries, where granted, to the applicable dates indicated in parentheses.

[d] The patent term extension ("PTE") system in Japan allows for a patent to be extended more than once provided the later approval is directed to a different indication from that of the previous approval. This may result in multiple PTE approvals for a given patent, each with its own expiration date. In this table, date ranges are shown for the expiration of Japanese patents for which multiple PTEs have been granted, with the later date indicating the latest expiring PTE for the corresponding patent.

[e] A patent term extension has been granted by the U.S. Patent and Trademark Office, extending the original patent term (October 2, 2027), insofar as it covers Dupixent, to March 28, 2031.

[f] This table excludes Japanese patents related to Praluent because Praluent is not being commercialized in Japan at this time.

[g] A patent term extension has been granted by the U.S. Patent and Trademark Office, extending the original patent term (June 1, 2027), insofar as it covers Kevzara, to May 22, 2031.

In addition to our patent portfolio, in the United States and certain other countries, our competitive position may be enhanced due to the availability of market exclusivity under relevant law (for additional information regarding market exclusivity, see Part I, Item 1A. "Risk Factors - Risks Related to Intellectual Property and Market Exclusivity - *Loss or limitation of patent rights, and regulatory pathways for biosimilar competition, could reduce the duration of market exclusivity for our products*"). The effect of expiration of a patent relating to a particular product also depends upon other factors, such as the nature of the market and the position of the product in it, the growth of the market, the complexities and economics of the process for manufacture of the active ingredient of the product, and the requirements of new drug provisions of the Federal Food, Drug and Cosmetic Act or similar laws and regulations in other countries.

We also are the nonexclusive licensee of a number of additional patents and patent applications. These include a license agreement with Bristol-Myers Squibb, E. R. Squibb & Sons, L.L.C., and Ono Pharmaceutical Co., Ltd. to obtain a license under certain patents owned and/or exclusively licensed by one or more of these parties that includes the right to develop and sell Libtayo. Under the agreement, we and Sanofi pay royalties of 8.0% on worldwide sales of Libtayo through December 31, 2023, and royalties of 2.5% from January 1, 2024 through December 31, 2026. The royalties are shared equally by us and Sanofi.

Patent law relating to the patentability and scope of claims in the biotechnology field is evolving and our patent rights are subject to this additional uncertainty. The degree of patent protection that will be afforded to our products in the United States and other important commercial markets is uncertain and is dependent upon the scope of protection decided upon by the patent offices, courts, and governments in these countries. There is no certainty that our existing patents or others, if obtained, will provide us protection from competition or provide commercial benefit.

Others may independently develop similar products or processes to those developed by us, duplicate any of our products or processes or, if patents are issued to us, design around any products and processes covered by our patents. We expect to continue, when appropriate, to file product and process applications with respect to our inventions. However, we may not file any such applications or, if filed, the patents may not be issued. Patents issued to or licensed by us may be infringed by the products or processes of others.

We seek to file and maintain trademarks around the world based on commercial activities in most jurisdictions where we have, or desire to have, a business presence for a particular product or service. Trademark protection varies in accordance with local law, and continues in some countries as long as the trademark is used and in other countries as long as the trademark is registered. Trademark registrations generally are for fixed but renewable terms.

Defense and enforcement of our intellectual property rights is expensive and time consuming, even if the outcome is favorable to us. It is possible that patents issued or licensed to us will be successfully challenged, that a court may find that we are infringing validly issued patents of third parties, or that we may have to alter or discontinue the development of our products or pay licensing fees to take into account patent rights of third parties (see Part I, Item 1A. "Risk Factors - Risks Related to Intellectual Property and Market Exclusivity - *We may be restricted in our development, manufacturing, and/or commercialization activities by patents or other proprietary rights of others, and could be subject to awards of damages if we are found to have infringed such patents or rights*"; and Note 15 to our Consolidated Financial Statements).

Government Regulation

Regulation by government authorities in the United States and foreign countries is a significant factor in the research, development, manufacture, and marketing of our products and our product candidates. A summary of the primary areas of government regulation that are relevant to our business is provided below. For a description of material regulatory risks we face, also refer to Part I, Item 1A. "Risk Factors."

Preclinical Requirements

The activities required before a product candidate may be marketed in the United States or elsewhere begin with preclinical tests. Preclinical tests include laboratory evaluations of, among other things, product chemistry and formulation and toxicological and pharmacological studies in animal species to assess the toxicity and dosing of the product candidate. In the United States, certain preclinical trials must comply with the FDA's Good Laboratory Practice requirements ("GLPs") and the U.S. Department of Agriculture's Animal Welfare Act. The results of these studies must be submitted to the FDA or the relevant regulatory authority outside the United States as part of an IND or clinical trial application (as applicable), which must be reviewed by the FDA or the relevant government authority before proposed clinical testing can begin in the applicable country or jurisdiction. In the United States, unless the FDA raises concerns, the IND becomes effective 30 days following its receipt by the FDA, and the clinical trial proposed in the IND may begin. The FDA or other regulatory authorities may ask for additional data in order to begin a clinical trial. Rules that are equivalent in scope but which vary in application apply in foreign countries.

Product Approval

All of our product candidates require regulatory approval by relevant government authorities before they can be commercialized. In particular, human therapeutic products are subject to rigorous preclinical and clinical trials and other pre-market approval requirements by the FDA and foreign authorities. The structure and substance of the FDA and foreign pharmaceutical regulatory practices may evolve over time. The ultimate outcome and impact of such developments cannot be predicted.

Clinical trials involve the administration of a drug to healthy human volunteers or to patients under the supervision of a qualified investigator. The conduct of clinical trials is subject to extensive regulation, including compliance with the FDA's bioresearch monitoring regulations and Good Clinical Practice requirements ("GCPs"), which establish standards for conducting, recording data from, and reporting the results of, clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. Clinical trials must be conducted under protocols that detail the study objectives, parameters for monitoring safety, and the efficacy criteria, if any, to be evaluated. In addition, each clinical trial must be reviewed and approved by, and conducted under the auspices of, an Institutional Review Board ("IRB") for each clinical site within the United States or, where applicable, an Ethics Committee and/or the competent authority for clinical sites outside the United States. Companies sponsoring the clinical trials, investigators, and IRBs/Ethics Committees also must comply with, as applicable, regulations and guidelines for obtaining informed consent from the study patients, following the protocol and investigational plan, adequately monitoring the clinical trial, and timely reporting of adverse events. Foreign studies conducted under an IND must meet the same requirements that apply to studies being conducted in the United States. Data from a foreign study not conducted under an IND may be submitted in support of a BLA if the study was conducted in accordance with GCPs and the FDA is able to validate the data. The sponsor of a clinical trial or the sponsor's designated responsible party may be required to register certain information about the trial and disclose certain results on government or independent registry websites, such as clinicaltrials.gov.

Typically, clinical testing involves a three-phase process, which may overlap or be subdivided in some cases. Phase 1 trials are usually conducted with a small number of healthy volunteers to determine the early safety profile, metabolism, and pharmacological actions of the product candidate, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. Although Phase 1 trials are typically conducted in healthy human subjects, in some instances, the trial subjects are patients with the targeted disease or condition. Phase 2 clinical trials are conducted with a relatively small sample of the intended patient population to provide enough data to evaluate the preliminary safety, tolerability, and efficacy of different potential doses of the product candidate. Phase 3 clinical trials are larger trials conducted with patients with the target disease or disorder intended to gather additional information about dosage, safety, and effectiveness necessary to evaluate the drug's overall risk-benefit profile. Phase 3 data often form the core basis on which the FDA and comparable foreign regulatory authorities evaluate a product candidate's safety and effectiveness when considering the product application for regulatory approval. If concerns arise about the safety of the product candidate, the FDA or other regulatory authorities can stop clinical trials by placing them on a "clinical hold" pending receipt of additional data, which can result in a delay or termination of a clinical development program. The sponsoring company, the FDA or other regulatory authorities, or the IRB or Ethics Committee and competent authority may suspend or terminate a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

The results of the preclinical and clinical testing of a biologic product candidate are then submitted to the FDA in the form of a BLA for evaluation to determine whether the product candidate may be approved for commercial sale under the Public Health Service Act. Under the Prescription Drug User Fee Act, we typically must pay fees to the FDA for review of any BLA. When a BLA is submitted, the FDA makes an initial determination as to whether the application is sufficiently complete to be accepted for review. If the application is not, the FDA may refuse to accept the BLA for filing and request additional information. A refusal to file, which requires resubmission of the BLA with the requested additional information, delays review of the application. If the application is accepted for review, the FDA reviews the application to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality, and purity.

FDA performance goals generally provide for action on a BLA within 10 months of the 60-day filing date (or within 12 months of the BLA submission). That deadline can be extended by FDA under certain circumstances, including by the FDA's requests for additional information. The targeted action date can be 6 months after the 60-day filing date (or 8 months after BLA submission) for product candidates that are granted priority review designation because they are intended to treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs. The FDA has other programs to expedite development and review of product candidates that address serious or life-threatening conditions.

For some BLAs, the FDA may convene an advisory committee to seek insights and recommendations on issues relevant to approval of the application. Although the FDA is not bound by the recommendation of an advisory committee, the agency considers such recommendations carefully when making decisions. Before approving a new drug or biologic product, the FDA

also requires that the facilities at which the product will be manufactured or advanced through the supply chain be in compliance with current Good Manufacturing Practices, or cGMP, requirements and regulations governing, among other things, the manufacture, shipment, and storage of the product. The FDA also can audit the sponsor of the BLA to determine if the clinical studies were conducted in compliance with current GCPs. After review of a BLA, the FDA may grant marketing approval, request additional information, or issue a complete response letter ("CRL") outlining the deficiencies in the submission. The CRL may require additional testing or information, including additional preclinical or clinical data, for the FDA to reconsider the application. Even if such additional information and data are submitted, the FDA may decide that the BLA still does not meet the standards for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than the sponsor. If FDA grants approval, an approval letter authorizes commercial marketing of the product candidate with specific prescribing information for specific indications.

Any approval required by the FDA for any of our product candidates may not be obtained on a timely basis, or at all. The designation of a clinical trial as being of a particular phase is not necessarily indicative that such a trial will be sufficient to satisfy the parameters of a particular phase, and a clinical trial may contain elements of more than one phase notwithstanding the designation of the trial as being of a particular phase. The results of preclinical studies or early stage clinical trials may not predict long-term safety or efficacy of our compounds when they are tested or used more broadly in humans. Additionally, as a condition of approval, the FDA may impose restrictions that could affect the commercial prospects of a product and increase our costs, such as a Risk Evaluation and Mitigation Strategy ("REMS") to mitigate certain specific safety risks, and/or post-approval commitments or requirements to conduct additional clinical trials or non-clinical studies or to conduct surveillance programs to monitor the product's effects.

Approval of a product candidate by comparable regulatory authorities in foreign countries is generally required prior to commencement of marketing of the product in those countries. The approval procedure varies among countries and may involve different or additional testing, and the time required to obtain such approval may differ from that required for FDA approval. Approval by a regulatory authority in one jurisdiction does not guarantee approval by comparable regulatory authorities in other jurisdictions. In the European Economic Area ("EEA") (which is comprised of 27 Member States of the EU plus Norway, Iceland, and Liechtenstein), medicinal products can only be commercialized after a related Marketing Authorization has been granted. Marketing authorization for biologics must be obtained through a centralized procedure, which allows a company to submit a single application to the EMA. If a related positive opinion is provided by the EMA, the EC will grant a centralized marketing authorization that is valid in the EEA.

In many jurisdictions, pediatric data or an approved Pediatric Investigation Plan ("PIP"), or a waiver of such studies, is required to have been approved by regulatory authorities prior to submission of a marketing application. In some EU countries, we may also be required to have an approved PIP before we can begin enrolling pediatric patients in a clinical trial. In the United States, under the Pediatric Research Equity Act ("PREA"), certain applications for approval must include an assessment, generally based on clinical study data, of the safety and effectiveness of the subject product in relevant pediatric populations, unless a waiver or deferral is granted. However, a pediatric study plan is not required for orphan products and the timing of the submission is subject to negotiation with FDA, but such plan cannot be submitted later than submission of a BLA.

Various federal, state, and foreign statutes and regulations also govern or influence the research, manufacture, safety, labeling, storage, record keeping, marketing, transport, and other aspects of developing and commercializing pharmaceutical product candidates. The lengthy process of seeking these approvals and the compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us or our collaborators or licensees to obtain, or any delay in obtaining, regulatory approvals could adversely affect the manufacturing or marketing of our products and our ability to receive product or royalty revenue.

For additional information regarding U.S. and foreign regulatory approval processes and requirements, see Part I, Item 1A. "Risk Factors - Risks Related to Maintaining Approval of Our Marketed Products and the Development and Obtaining Approval of Our Product Candidates and New Indications for Our Marketed Products - *Obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain.*"

Emergency Use Authorization

The Secretary of HHS may authorize unapproved medical products to be marketed in the context of an actual or potential emergency that has been designated by the U.S. government. The COVID-19 pandemic has been designated as such a national emergency. After an emergency has been announced, the Secretary of HHS may authorize the issuance of, and the FDA Commissioner may issue, EUAs for the use of specific products based on criteria established by the Food, Drug, and Cosmetic Act, including that the product at issue may be effective in diagnosing, treating, or preventing serious or life-threatening diseases when there are no adequate, approved, and available alternatives. Although the criteria of an EUA differ from the criteria for approval of a BLA, EUAs nevertheless require the development and submission of data to satisfy the relevant FDA standards, as well as a number of ongoing compliance obligations. The FDA expects EUA holders to work toward submission of full

applications, such as a BLA, as soon as possible. An EUA is also subject to additional conditions and restrictions and is product-specific. An EUA terminates when the emergency determination underlying the EUA terminates. An EUA is not a long-term alternative to obtaining FDA approval, licensure, or clearance for a product. The FDA may revoke, revise, or restrict an EUA for a variety of reasons, including where it is determined that the underlying health emergency no longer exists or warrants such authorization or the medical product is no longer effective in diagnosing, treating, or preventing the underlying health emergency.

Post-Approval Regulation

The FDA and comparable regulatory authorities in other jurisdictions may also require us to conduct additional clinical trials or to make certain changes related to a product after granting approval of the product. The FDA has the explicit authority to require postmarketing studies (also referred to as post-approval or Phase 4 studies) and labeling changes based on new safety information, and may impose and enforce a REMS at the time of approval or after the product is on the market. Post-approval modifications to the drug, such as changes in indications, labeling, or manufacturing processes or facilities, may require a sponsor to develop additional data or conduct additional preclinical studies or clinical trials, to be submitted in a new or supplemental BLA, which would require FDA approval.

Following approval, the FDA and comparable regulatory authorities outside the United States regulate the marketing and promotion of our products, which must comply with the Food, Drug, and Cosmetic Act and applicable FDA regulations and standards thereunder and equivalent foreign laws. The review of promotional activities by the FDA and comparable regulatory authorities outside the United States includes, but is not limited to, healthcare provider-directed and direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, promotional activities involving the Internet, and sales representatives' communications. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA and comparable foreign regulatory authorities. FDA and comparable foreign regulatory authorities' regulations impose restrictions on manufacturers' communications regarding unapproved uses, but under certain conditions may engage in non-promotional, balanced, scientific communication regarding such use. Failure to comply with applicable FDA and comparable foreign regulatory authorities' requirements and restrictions in this area may subject a company to adverse publicity and enforcement action by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities and comparable regulatory authorities outside the United States. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes a drug. See Part I, Item 1A. "Risk Factors - Other Regulatory and Litigation Risks - *Our business activities have been, and may in the future be, challenged under federal or state healthcare laws, which may subject us to civil or criminal proceedings, investigations, or penalties*."

Adverse-event reporting and submission of periodic reports are required following marketing approval. The FDA requires BLA holders to employ a system for obtaining and reviewing safety information, adverse events, and product complaints associated with each drug and to submit safety reports to the FDA, with expedited reporting timelines in certain situations. Based on new safety information after approval, the FDA can, among other things, mandate product labeling changes, require new post-marketing studies, impose or modify a risk evaluation and mitigation strategy for the product, or suspend or withdraw approval of the product. We may be subject to audits by the FDA and other regulatory authorities to ensure that we are complying with the applicable requirements. Rules that are equivalent in scope but which vary in application apply in foreign countries in which we conduct clinical trials.

The holder of an EU marketing authorization for a medicinal product must also comply with the EU's pharmacovigilance legislation. This includes requirements to conduct pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. Marketing authorization holders are required to maintain a Pharmacovigilance System Master File ("PSMF"), which supports and documents the compliance of the marketing authorization holder with the requirements of EU pharmacovigilance legislation. Marketing authorization holders are also required to have a Qualified Person for Pharmacovigilance ("QPPV"), who, among other things, maintains the PSMF. A QPPV must reside in the EEA and must also prepare pharmacovigilance reports, respond to potential requests from competent authorities concerning pharmacovigilance on a 24 hour basis, and provide competent authorities with any other information that may be relevant to the safety of the medicinal product in accordance with Good Pharmacovigilance Practices.

The EC can also require marketing authorization holders to conduct post-authorization safety and/or efficacy studies. A post-authorization safety study ("PASS") is a study that is carried out after a medicinal product has been authorized to obtain further information on a medicinal product's safety, or to measure the effectiveness of risk-management measures. Such studies may be clinical trials or non-interventional studies. A post-authorization efficacy study ("PAES") is a study that is carried out for complementing available efficacy data in the light of well-reasoned scientific uncertainties on aspects of the evidence of benefits that is to be or only can be addressed post-authorization. The EC may, in particular, impose a PASS and/or PAES on marketing authorization holders when a marketing authorization is granted upon conditions. The EC may grant conditional marketing

authorizations in the interest of public health, when there is less comprehensive clinical data available than would be required, if the EC considers that the benefit of immediate availability may outweigh the risk that the absence of the required clinical data poses.

In addition, we and our third-party suppliers are required to maintain compliance with cGMP, and are subject to inspections by the FDA or comparable regulatory authorities in other jurisdictions to confirm such compliance. Changes of suppliers or modifications of methods of manufacturing may require amending our application(s) to the FDA or such comparable foreign regulatory authorities and acceptance of the change by the FDA or such comparable foreign regulatory authorities prior to release of product(s). FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and our third-party suppliers. Prescription drug manufacturers in the U.S. must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities, and have procedures in place to identify and properly handle suspect and illegitimate products. We may also be subject to state regulations related to the manufacturing and distribution of our products.

Failure to comply with these laws, regulations, and conditions of product approval may lead the FDA and comparable regulatory authorities in other jurisdictions to take regulatory action or seek sanctions, including fines, issuance of warning letters, civil penalties, injunctions, suspension of manufacturing operations, operating restrictions, withdrawal of FDA approval of a product, seizure or recall of products, and criminal prosecution.

Pricing and Reimbursement

Sales in the United States of our marketed products are dependent, in large part, on the availability and extent of reimbursement from third-party payors, including private payor healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid. Sales of our marketed products in other countries are dependent, in large part, on coverage and reimbursement mechanisms and programs administered by health authorities in those countries. See Part I, Item 1A. "Risk Factors - Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *Sales of our marketed products are dependent on the availability and extent of reimbursement from third-party payors, and changes to such reimbursement may materially harm our business, prospects, operating results, and financial condition.*"

We participate in, and have certain price reporting obligations to, the Medicaid Drug Rebate program, state Medicaid supplemental rebate program(s), and other governmental pricing programs. We also have obligations to report the average sales price for certain drugs to the Medicare program as part of our agreement to participate in the Medicaid Drug Rebate program. For calendar quarters beginning January 1, 2022, we will be required to report the average sales price for certain drugs under the Medicare program regardless of whether we participate in the Medicaid Drug Rebate Program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available for our drugs under Medicaid and Part B of the Medicare program.

Medicaid is a joint federal and state program that is administered by the states for low-income and disabled beneficiaries. Medicaid rebates are based on pricing data reported by us on a monthly and quarterly basis to the Centers for Medicare & Medicaid Services ("CMS"), the federal agency that administers the Medicaid and Medicare programs. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. The amount of the rebate is adjusted upward if average manufacturer price increases more than inflation (measured by reference to the Consumer Price Index - Urban). Currently, the rebate is capped at 100 percent of the average manufacturer price, but effective January 1, 2024, this cap on the rebate will be removed, and our rebate liability could increase accordingly.

If we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due, which revisions could affect our rebate liability for prior quarters. The federal Patient Protection and Affordable Care Act (the "PPACA") made significant changes to the Medicaid Drug Rebate program, and CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the PPACA. On December 21, 2020, CMS issued a final rule that modified Medicaid Drug Rebate program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements (beginning in 2022); provide definitions for "line extension," "new formulation," and related terms with the practical effect of expanding the scope of drugs considered to be line extensions (beginning in 2022); and revise best price and average manufacturer price exclusions of manufacturer-sponsored patient benefit programs, particularly regarding potential inapplicability of such exclusions in the context of pharmacy benefit manager "accumulator" programs (beginning in 2023).

Medicare is a federal program that is administered by the federal government that covers individuals age 65 and over or that are disabled as well as those with certain health conditions. Medicare Part B generally covers drugs that must be administered by physicians or other health care practitioners; are provided in connection with certain durable medical equipment; or are certain oral anti-cancer drugs and certain oral immunosuppressive drugs. Medicare Part B pays for such drugs under a payment methodology based on the average sales price of the drugs. Manufacturers, including us, are required to report average sales price information to CMS on a quarterly basis. The manufacturer-submitted information is used by CMS to calculate Medicare payment rates. Starting in 2023, manufacturers must pay refunds to Medicare for single-source drugs or biological products, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125 percent of the refund amount.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false pricing or other information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, or if we fail to submit the required data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing program (the "340B program") in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the Health Resources and Services Administration ("HRSA"), requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. Covered entities include hospitals that serve a disproportionate share of financially needy patients, community health clinics, and other entities that receive certain types of grants under the Public Health Service Act. The PPACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers, and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under this regulation. Any charge by HRSA that we have violated the requirements of the regulation could result in civil monetary penalties. Moreover, under a final regulation effective January 13, 2021, HRSA established a new administrative dispute resolution ("ADR") process for claims by covered entities that a manufacturer has engaged in overcharging, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. An ADR proceeding could subject us to onerous procedural requirements and could result in additional liability. HRSA also implemented a price reporting system under which we are required to report our 340B ceiling prices to HRSA on a quarterly basis, which then publishes those prices to 340B covered entities. In addition, legislation could be passed that would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. FSS participation is required for our products to be purchased by the VA, Department of Defense ("DoD"), Coast Guard, and Public Health Service ("PHS"). Prices for innovator drugs purchased by the VA, DoD, Coast Guard, and PHS are subject to a cap (known as the "Federal Ceiling Price") equal to 76% of the annual non-federal average manufacturer price ("non-FAMP") minus, if applicable, an additional discount. The additional discount applies if non-FAMP increases more than inflation (measured by reference to the Consumer Price Index - Urban). We also participate in the Tricare Retail Pharmacy Program, under which we pay quarterly rebates to DoD for prescriptions of our innovator drugs dispensed to Tricare beneficiaries through Tricare Retail network pharmacies. The governing statute provides for civil monetary penalties for failure to provide information timely or for knowing submission of false information to the government.

Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that are not administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and, subject to detailed program rules and government oversight, each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time. The prescription drug plans negotiate pricing with manufacturers and pharmacies, and may condition formulary placement on the availability of manufacturer discounts. In addition, for 2021, manufacturers, including us, are required to provide to CMS a 70% discount on brand name

prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries are in the coverage gap phase of the Part D benefit design.

Private payor healthcare and insurance providers, health maintenance organizations, and pharmacy benefit managers in the United States are adopting more aggressive utilization management techniques and are increasingly requiring significant discounts and rebates from manufacturers as a condition to including products on formulary with favorable coverage and copayment/ coinsurance. These payors may not cover or adequately reimburse for use of our products or may do so at levels that disadvantage them relative to competitive products.

Outside the United States, within the EU, our products are paid for by a variety of payors, with governments being the primary source of payment. Government health authorities in the EU determine or influence reimbursement of products, and set prices or otherwise regulate pricing. Negotiating prices with governmental authorities can delay commercialization of our products. Governments may use a variety of cost-containment measures to control the cost of products, including price cuts, mandatory rebates, value-based pricing, and reference pricing (i.e., referencing prices in other countries or prices of competitive products and using those reference prices to set a price). Budgetary pressures in many EU countries are continuing to cause governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates, and expanded generic substitution and patient cost-sharing.

Other Regulatory Requirements

We are subject to health care "fraud and abuse" laws, such as the federal civil False Claims Act, the anti-kickback provisions of the federal Social Security Act, and other state and federal laws and regulations. Federal and state anti-kickback laws prohibit, among other things, payments or other remuneration to induce or reward someone to purchase, prescribe, endorse, or recommend a product that is reimbursed under federal or state healthcare programs. Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds, or knowingly making, or causing to be made, a false statement to get a false claim paid. See Part I, Item 1A. "Risk Factors - Other Regulatory and Litigation Risks - *Our business activities have been, and may in the future be, challenged under federal or state healthcare laws, which may subject us to civil or criminal proceedings, investigations, or penalties*."

We are subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. See Part I, Item 1A. "Risk Factors - Other Regulatory and Litigation Risks - *Risks from the improper conduct of employees, agents, contractors, or collaborators could adversely affect our reputation and our business, prospects, operating results, and financial condition*."

In the United States, there are numerous federal and state laws and regulations governing data privacy of personal data and the collection, use, disclosure, and protection of health data, genetic data, consumer data, and children's data. Such laws and regulations include the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (collectively, "HIPAA"), as well as state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (such as Section 5 of the Federal Trade Commission Act and the California Consumer Privacy Act (the "CCPA")). Many of these laws differ from each other in significant ways and have different effects. Many of the state laws enable a state attorney general to bring actions and provide private rights of action to consumers as enforcement mechanisms. There is also heightened sensitivity around certain types of health data, which may be subject to additional protections. The landscape of federal and state laws regulating personal data is constantly evolving. Failure to comply with these laws and regulations could result in government enforcement actions and create liability for us (which could include civil and/or criminal penalties), private litigation, and/or adverse publicity. Federal regulators, state attorneys general, and plaintiffs' attorneys have been active in this space.

HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their "business associates" – certain persons or covered entities that create, receive, maintain, or transmit protected health information ("PHI") in connection with providing a specified service or performing a function on behalf of a covered entity. Most health care providers, including research institutions from which we or our collaborators obtain clinical trial data, are subject to HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive, use, or disclose PHI maintained by a HIPAA-covered entity in a manner that is not permitted under HIPAA.

To the extent we collect California resident personal data, we are also subject to the CCPA. The CCPA, which became effective on January 1, 2020, created new transparency requirements and granted California residents several new rights with regard to their personal data. In addition, in November 2020, California voters approved the California Privacy Rights Act ("CPRA") ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency ("CPPA"). The amendments introduced by the CPRA go into effect on January 1, 2023, and new implementing regulations are expected to be introduced by the CPPA. Failure to comply with the CCPA

may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages. Similarly, there are a number of legislative proposals in the United States, at both the federal and state level, that could impose new obligations or limitations in the area of consumer protection. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws.

Outside the United States, our clinical trial programs, research collaborations, and other processing activities implicate international data protection laws, including the EU General Data Protection Regulation 2016/679 ("GDPR"). The GDPR has increased our responsibility and liability in relation to the processing of personal data of individuals located in the EU. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze, and transfer personal data, including health data and samples from clinical trials and adverse event reporting. In particular, these obligations and restrictions may concern the consent of the individuals to whom the personal data relate, the information provided to the individuals, the sharing of personal data with third parties, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for violations of the data protection obligations. With respect to the transfer of personal data outside of the EU, while there are legal mechanisms available to lawfully transfer personal data outside of the EU, including to the United States, there are certain unsettled legal issues regarding such data transfers, the resolution of which may adversely affect our ability to transfer personal data or otherwise may cause us to incur significant costs to come into compliance with applicable data transfer impact assessments and implementation of legal data transfer mechanisms. In June 2021, the European Commission published new standard contractual clauses required to be incorporated into new and existing agreements within prescribed timeframes in order to continue to lawfully transfer personal data outside of the EU. Different EU member states, as well as the United Kingdom and Switzerland, have promulgated national privacy laws that impose additional requirements, which add to the complexity of processing and transferring EU personal data. Some countries outside of the EU have reacted to the GDPR by promulgating and enacting new privacy legislation that reflects similar principals and obligations on companies that operate and process their citizens' personal data. Any failure or perceived failure to comply with privacy-related legal obligations, or any compromise of security of personal data, may result in governmental enforcement actions, litigation, contractual indemnity claims, or restraining orders that would impact our ability to process and share data globally. As we expand our presence into new countries, we must continue to assess our privacy controls to enable the processing of personal data. Guidance on implementation and compliance practices are often updated or otherwise revised. See Part I, Item 1A. "Risk Factors - Other Regulatory and Litigation Risks - *We face risks related to the personal data we collect, process, and share*."

In addition to the foregoing, our present business is, and our future business may be, subject to regulation under the United States Atomic Energy Act, the Clean Air Act, the Clean Water Act, the Comprehensive Environmental Response, Compensation and Liability Act, the National Environmental Policy Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, national restrictions, and other current and potential future local, state, federal, and foreign regulations.

Business Segments

We manage our business as one segment which includes all activities related to the discovery, development, and commercialization of medicines for serious diseases. For financial information related to our one segment, see our Consolidated Financial Statements and related notes.

Human Capital Resources

We compete in the highly competitive biotechnology and pharmaceuticals industries. Attracting, developing, and retaining skilled and experienced employees in research and development, manufacturing, sales and marketing, and other positions is crucial to our ability to compete effectively. Our ability to recruit and retain such employees depends on a number of factors, including our corporate culture and work environment, informed by our values and behaviors (which we call The Regeneron Way) and our corporate philosophy of "Doing Well by Doing Good"; talent development and career opportunities; and compensation and benefits.

Employee Profile

As of December 31, 2021, we had 10,368 full-time employees, consisting of 8,564 employed in the United States, 1,648 employed in Ireland, and 156 employed in other countries (including the United Kingdom, Germany, the Netherlands, and Canada). Of these employees, 1,936 were within our research and preclinical development organization, 1,300 were within our global clinical development organization, and 5,037 were within our industrial operations and product supply organization. Company-wide, nearly 1,200 of our full-time employees hold a Ph.D. and/or M.D. None of our employees are represented by a labor union, and our management considers its relations with our employees to be good.

Diversity, Equity, and Inclusion

Our employees represent a broad range of backgrounds, just like the people who take our medicines, and bring a wide array of perspectives and experiences that have helped us achieve our leadership position in the biotechnology and pharmaceuticals industries and the global marketplace. A key component of our corporate culture is our commitment to the promotion of diversity, equity, and inclusion ("DEI"). We believe this commitment allows us to better drive innovation and achieve our mission to repeatedly bring important new medicines to patients with serious diseases. Our DEI principles are reflected in our efforts in building a better workplace where employees can be themselves and succeed, advance medicine for all with better science, and use their voice and influence to create a better world. We empower employee-led cross-functional resource groups ("ERGs") and interest groups, who connect around a common passion to build a culture of inclusion and collaborate to support under-served science and global communities. In 2021, we launched several new ERGs, all of which align their objectives to our global DEI strategy and provide meaningful professional development opportunities for our workforce, with support from senior leaders as executive sponsors.

While we are proud of our workforce diversity representation shown in the table below, we seek to continuously improve in this area. In April 2020, we announced our 2025 global responsibility goals, including a commitment to increase diversity in leadership and foster inclusion. Making progress toward this goal, in 2020, we established a DEI steering committee of senior leaders to provide oversight and guidance on our DEI efforts. In 2021, we hired our Chief DEI Officer; launched a DEI strategy focused on creating a better workplace, better science, and better world; and implemented a new governance model that includes both an executive DEI council and a DEI leadership council. These councils are comprised of senior leaders who provide oversight and guidance on our DEI efforts and support the execution of our DEI strategy. In order to better understand our employees' perspectives, we also conducted an employee engagement survey and launched an objective measure for inclusion and belonging. Our board of directors received a detailed update on our DEI efforts in 2021 and continues to monitor our progress.

2021 Workforce Diversity Representation*

Female Representation (Global)	49.3 %
Minority Representation (U.S. Only)**	23.6 %

* Based on full-time employees as of December 31, 2021

** Represents the percentage of our full-time employees in the United States that self-identified as belonging to a racial or ethnic minority group. The denominator used in this calculation includes employees who did not disclose information related to their race or ethnicity. Excluding those that did not disclose such information, the percentage shown in this table would be 31.0%.

Externally, we support DEI efforts in our community, including by supporting young scientific talent in underrepresented communities. For example, through our partnership with the Society for Science, we contribute a substantial amount annually to science, technology, engineering, and mathematics ("STEM") equity and outreach programs to help increase access to science research education and bridge opportunity gaps among students historically underrepresented in the sciences. We also continue to take steps to further integrate diversity considerations into the design and selection of sites for our clinical studies to make sure they reflect the diversity of patients with the diseases under investigation.

Employee Wellness, Health, and Safety

The wellbeing of our employees is a primary focus as we believe that the most productive people are those who are at their best, both physically and mentally. We provide several programs related to employee health and wellness, including onsite amenities and programs such as meditation and prayer rooms and fitness centers. Throughout the COVID-19 pandemic, we have continued to prioritize mental health initiatives and take further action to reduce or remove barriers to quality mental healthcare for our employees and their family members. We also provide support for work-life balance through flex-time, remote working arrangements, child and elder care, and paid parental leave, among others.

Occupational health and safety is critical to our success. We are committed to meeting or exceeding all environmental, health, safety ("EHS"), and security regulations and have a range of programs, plans, and procedures to ensure the safety of all people who come to work at Regeneron. In addition, our 2025 global responsibility goals include a commitment to focus on workplace injury prevention in our drive toward zero incidents.

In response to the COVID-19 pandemic, we implemented changes in our business beginning in March 2020 to protect our employees and support appropriate health and safety protocols, such as work-from-home policies for a significant portion of our employees, increased physical distancing in workspaces, and regular testing. As the dynamics of the COVID-19 pandemic continue to evolve, we adjust and tailor our approach based on public health guidance and local community case rates. For our essential employees who remain onsite in our laboratories and manufacturing facilities, we provide personal protective equipment

and require masks to be worn. For any employee who contracts or is exposed to COVID-19, we provide full pay for their entire recovery and quarantine time. In addition, we have established a workforce reintegration plan to facilitate our large-scale return to office. The reintegration plan includes safety measures and procedures in compliance with local, state, and federal mandates.

Employee Growth and Development

We invest significant resources to develop talent with the right capabilities to deliver the growth and innovation needed to support our continued success. Our Talent department is dedicated to promoting individual, leader, team, and organizational development through a number of tools and services. We offer a variety of professional development courses for our employees and support employee continuing education, including through educational reimbursement and tuition forgiveness programs. In addition, we continue to invest in our current and future leaders through a number of leadership development courses and programs and feedback and coaching opportunities. In 2021, over 25% of job openings were filled by existing employees who were seeking career development opportunities.

Employee Engagement

We believe engaging our employees, from their first day and throughout their career, is key to fostering new ideas and driving commitment and productivity. We communicate frequently and transparently with our employees through a variety of communication methods, including video and written communications, company forums and summits, annual engagement surveys, and pulse surveys.

We are also committed to fostering employee volunteerism to reach our 2025 global responsibility goal of driving employee volunteer levels above national standards. Employees are encouraged and empowered to support organizations and causes that are important to them including through, among other things, our matching gift program, volunteer-time-off policy, and our annual company-wide service event, *Day for Doing Good*. In order to make progress on this goal during the COVID-19 pandemic, we transitioned volunteer programs to virtual formats to continue to support our non-profit partners while safeguarding health and safety.

The success of our employee engagement efforts is demonstrated by our employee retention rate of 92.2% in 2021, as well as the fact that nearly 90% of our employees who responded to our annual engagement survey said Regeneron is a great place to work, of which we are especially proud since over 30% of our current workforce was onboarded during the COVID-19 pandemic. Additionally, for the seventh consecutive year, we were recognized on the *Fortune* "100 Best Companies to Work For" list in 2021. We have also placed in the top five for the past 11 years in *Science* magazine's annual "Top Employers Survey" of the global biotechnology and pharmaceutical industry.

Compensation and Benefits

We are committed to rewarding and supporting our employees in order to continue to attract and retain top talent. We believe this commitment supports our core strategy of creating and advancing a high-quality product pipeline and delivering medicines to people in need. Employee engagement, commitment, and achievements are key drivers of pipeline success and therefore our long-term performance. The primary underpinning of our pay philosophy is to award equity-based pay to all eligible employees to ensure that when we deliver for patients and for shareholders, everyone shares in the upside growth. Our practice, therefore, has been to award initial equity grants to all new hires, in addition to our comprehensive annual equity program. Total employee compensation packages (which varies by country and region) include market-competitive pay (with the opportunity to receive above-market rewards), broad-based grants of equity-based awards, comprehensive healthcare benefits, and retirement savings options and matching contributions. We annually review our workforce demographic and pay equity data to track our performance and inform new initiatives.

Corporate Information

We were incorporated in the State of New York in 1988 and publicly listed in 1991. Our principal executive offices are located at 777 Old Saw Mill River Road, Tarrytown, New York 10591, and our telephone number at that address is (914) 847-7000.

We make available free of charge on or through our Internet website (*http://www.regeneron.com*) our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and, if applicable, amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission ("SEC").

Investors and other interested parties should note that we use our media and investor relations website (*http://newsroom.regeneron.com*) and our social media channels to publish important information about Regeneron, including information that may be deemed material to investors. We encourage investors and other interested parties to review the

information we may publish through our media and investor relations website and the social media channels listed on our media and investor relations website, in addition to our SEC filings, press releases, conference calls, and webcasts.

The information contained on our websites and social media channels is not included as a part of, or incorporated by reference into, this report.

ITEM 1A. RISK FACTORS

We operate in an environment that involves a number of significant risks and uncertainties. We caution you to read the following risk factors, which have affected, and/or in the future could affect, our business, prospects, operating results, and financial condition. The risks described below include forward-looking statements, and actual events and our actual results may differ materially from these forward-looking statements. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also impair our business, prospects, operating results, and financial condition. Furthermore, additional risks and uncertainties are described under other captions in this report and should also be considered by our investors. For purposes of this section (as well as this report in general), references to our products encompass products marketed or otherwise commercialized by us and/or our collaborators or licensees and references to our product candidates encompass product candidates in development by us and/or our collaborators or licensees (in the case of collaborated or licensed products or product candidates under the terms of the applicable collaboration or license agreements), unless otherwise stated or required by the context. In this section, we first provide a summary of the more significant risks and uncertainties we face and then provide a full set of risk factors and discuss them in greater detail.

Summary of Risk Factors

As noted above, we are subject to a number of risks that if realized could materially harm our business, prospects, operating results, and financial condition. Some of the more significant risks and uncertainties we face include those summarized below. The summary below is not exhaustive and is qualified by reference to the full set of risk factors set forth in this "Risk Factors" section. Please carefully consider all of the information in this Form 10-K, including the full set of risks set forth in this "Risk Factors" section, and in our other filings with the SEC before making an investment decision regarding Regeneron.

Risks Related to the COVID-19 Pandemic

- Our business may be further adversely affected by the effects of the COVID-19 pandemic, including those impacting our manufacturing and supply chain operations, research and development efforts, commercial operations and sales force, administrative personnel, third-party service providers, and business partners and customers, as well as the demand for our marketed products.
- We face risks related to the development, manufacturing, and commercialization of REGEN-COV and "next generation" monoclonal antibodies targeting SARS-CoV-2.

Commercialization Risks

- We are substantially dependent on the success of EYLEA and Dupixent.
- Sales of our products are dependent on the availability and extent of reimbursement from third-party payors, including private payors and government programs such as Medicare and Medicaid, which could change due to various factors such as drug price control measures that have been or may be introduced in the United States by various federal and state authorities.
- The commercial success of our products is subject to significant competition from products or product candidates that may be superior to, or more cost effective than, our products or product candidates.
- We and our collaborators on which we rely to commercialize some of our marketed products may be unable to continue to successfully commercialize or co-commercialize our products, both in the United States and abroad.

Regulatory and Development Risks

- Drug development and obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain.
- Serious complications or side effects in connection with the use or development of our products or product candidates could cause our regulatory approvals to be revoked or limited or lead to delay or discontinuation of development of our product candidates or new indications for our marketed products.
- We may be unable to formulate or manufacture our product candidates in a way that is suitable for clinical or commercial use, which would delay or prevent continued development of such candidates and/or receipt of regulatory approval or commercial sale.
- Many of our products are intended to be used in combination with drug-delivery devices, which may result in additional regulatory, commercialization, and other risks.

Intellectual Property and Market Exclusivity Risks

- We may not be able to protect the confidentiality of our trade secrets, and our patents or other means of defending our intellectual property may be insufficient to protect our proprietary rights.
- Patents or proprietary rights of others may restrict our development, manufacturing, and/or commercialization efforts and subject us to patent litigation and other proceedings that could find us liable for damages.
- Loss or limitation of patent rights, and regulatory pathways for biosimilar competition, could reduce the duration of market exclusivity for our products, including EYLEA.

Manufacturing and Supply Risks

- We rely on limited internal and contracted manufacturing and supply chain capacity, which could adversely affect our ability to commercialize our products and to advance our clinical pipeline. As we increase our production in response to higher product demand or in anticipation of a potential regulatory approval, our current manufacturing capacity will likely not be sufficient, and our dependence on our collaborators and/or contract manufacturers may increase, to produce adequate quantities of drug material for both commercial and clinical purposes.
- Expanding our manufacturing capacity and establishing fill/finish capabilities will be costly and we may be unsuccessful in doing so in a timely manner, which could delay or prevent the launch and successful commercialization of our products approved for marketing and could jeopardize our clinical development programs.
- Our ability to manufacture products may be impaired if any of our or our collaborators' manufacturing activities, or the activities of other third parties involved in our manufacture and supply chain, are found to infringe patents of others.
- If sales of our marketed products do not meet the levels currently expected, or if the launch of any of our product candidates is delayed or unsuccessful, we may face costs related to excess inventory or unused capacity at our manufacturing facilities and at the facilities of third parties or our collaborators.
- Third-party service or supply failures, failures at our manufacturing facilities in Rensselaer, New York and Limerick, Ireland, or failures at the facilities of any other party participating in the supply chain, would adversely affect our ability to supply our products.
- Our or our collaborators' failure to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates could result in incurring substantial remedial costs, delays in the development or approval of our product candidates or new indications for our marketed products and/or in their commercial launch if regulatory approval is obtained, and a reduction in sales.

Other Regulatory and Litigation Risks

- If the testing or use of our products harms people, or is perceived to harm them even when such harm is unrelated to our products, we could be subject to costly and damaging product liability claims.
- Our business activities have been, and may in the future be, challenged under federal or state healthcare laws, which may subject us to civil or criminal proceedings, investigations, or penalties.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions, and fines.
- We face risks from the improper conduct of our employees, agents, contractors, or collaborators, including those relating to potential non-compliance with relevant laws and regulations such as the Foreign Corrupt Practices Act and the U.K. Bribery Act.
- Our operations are subject to environmental, health, and safety laws and regulations, including those governing the use of hazardous materials.
- Changes in laws and regulations affecting the healthcare industry could adversely affect our business.
- Tax liabilities and risks associated with our operations outside of the United States could adversely affect our business.
- We face risks related to the personal data we collect, process, and share.

Risks Related to Our Reliance on Third Parties

- If our collaborations with Sanofi or Bayer are terminated or breached, our ability to develop, manufacture, and commercialize certain of our products and product candidates in the time expected, or at all, would be materially harmed.
- Our collaborators and service providers may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of our drug candidates and current and future products.

Other Risks Factors – Risks Related to Employees, Information Technology, Financial Results and Liquidity, and Our Common Stock

- Our business is dependent on our key personnel and will be harmed if we cannot recruit and retain leaders in our research, development, manufacturing, and commercial organizations.
- Significant disruptions of information technology systems or breaches of data security could adversely affect our business.
- We may need additional funding in the future, which may not be available to us, and which may force us to delay, reduce, or eliminate our product development programs or commercialization efforts.
- Our indebtedness could adversely impact our business.
- Our stock price is extremely volatile.
- Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval and over our management.

* * *

Risks Related to the COVID-19 Pandemic

Our business may be further adversely affected by the effects of the COVID-19 pandemic.

In December 2019, a novel strain of coronavirus, SARS-CoV-2, causing a disease referred to as COVID-19, was reported to have surfaced in Wuhan, China. It has since spread around the world and caused a global pandemic. This pandemic has adversely affected or has the potential to adversely affect, among other things, the economic and financial markets and labor resources of the countries in which we operate; our manufacturing and supply chain operations, research and development efforts, commercial operations and sales force, administrative personnel, third-party service providers, and business partners and customers; and the demand for our marketed products.

The COVID-19 pandemic has resulted in the imposition of various restrictions and mandates around the world to reduce the spread of the disease, including governmental orders that direct individuals to shelter at their places of residence, direct businesses and governmental agencies to cease non-essential operations at physical locations, prohibit certain non-essential gatherings, maintain social distancing, order cessation of non-essential travel, and require proof of vaccination and/or negative COVID-19 test results. The COVID-19 pandemic has continued to ebb and flow, with different jurisdictions having higher levels of infections than others and new variants of the SARS-CoV-2 virus (such as the Omicron variant) emerging and spreading more easily and quickly than other variants. As the pandemic continues to rapidly evolve, its ultimate impact is highly uncertain and subject to change and we do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems, or the global economy as a whole. These effects could have a material impact on our operations.

By way of example, continuation or re-imposition of various government-imposed or private-sector measures relating to the COVID-19 pandemic (including those we previously implemented, such as work-from-home policies for some employees) may further negatively impact productivity, disrupt our business, and delay our clinical programs and development timelines beyond the delays we have already experienced and disclosed. Such restrictions and limitations may also further negatively impact our access to regulatory authorities (which are affected, among other things, by applicable travel restrictions and may be delayed in responding to inquiries, reviewing filings, and conducting inspections); our ability to perform regularly scheduled quality checks and maintenance; and our ability to obtain services from third-party specialty vendors and other providers or to access their expertise as fully and timely as needed. The COVID-19 pandemic may also result in the loss of some of our key personnel, either temporarily or permanently. We and our employees may also be subject to government vaccine mandates, such as President Biden's recent Executive Order entitled "Executive Order on Ensuring Adequate COVID Safety Protocols for Federal Contractors" applicable to certain federal contractors. While enforcement of this mandate is currently enjoined and a similar mandate was recently struck down by the United States Supreme Court, if this mandate or any similar mandate becomes applicable to us, it may have a negative impact on our ability to retain employees or hire new employees and could adversely impact our business. In addition, our sales and marketing efforts were previously negatively impacted and may be further negatively impacted by postponement or cancellation of face-to-face meetings and restrictions on access by non-essential personnel to hospitals or clinics to the extent such measures slow down adoption or further commercialization of our marketed products. The demand for our marketed products may also be adversely impacted by the restrictions and limitations adopted in response to the COVID-19 pandemic, particularly to the extent they affect the patients' ability or willingness to start or continue treatment with our marketed products. Any of the foregoing factors may result in lower net product sales of our marketed products. For example, net product sales of EYLEA in the United States decreased for the three months ended June 30, 2020, compared to the same period in 2019, due in part to the impact of the COVID-19 pandemic. See Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Results of Operations" for a discussion of our net product sales. Demand for some or all of our marketed products may be further reduced if shelter-in-place, social distancing, or

similar orders remain in effect or are re-implemented and, as a result, some of our inventory may become obsolete and may need to be written off, impacting our operating results. These and similar, and perhaps more severe, disruptions in our operations may materially adversely impact our business, operating results, and financial condition.

Various government-imposed or private-sector measures relating to the COVID-19 pandemic (or the perception that such restrictions or limitations on the conduct of business operations could occur) previously impacted, and may impact in the future, personnel at our research and manufacturing facilities, our suppliers, and other third parties on which we rely, as well as the availability or cost of materials produced by or purchased from such parties, resulting in supply chain strains or disruptions that may become material. While some materials and services may be obtained from more than one supplier or provider, port closures and other restrictions, whether resulting from the COVID-19 pandemic or otherwise (including any government restrictions or limitations, such as those that may be imposed under the Defense Production Act), could materially disrupt our supply chain or limit our ability to obtain sufficient materials or services (including fill/finish services) required for the development and manufacturing of our products and product candidates as well as our research efforts. If microbial, viral (including COVID-19), or other contaminations are discovered in our products, product candidates, the materials used for their production, or in our facilities, or in the facilities of our collaborators, third-party contract manufacturers, or other providers or suppliers, the affected facilities may need to be closed or may otherwise be affected for an extended period of time, or the contamination may result in other delays or disruptions in our direct or indirect supply chain.

In addition, infections, hospitalizations, and deaths related to COVID-19 previously disrupted and may in the future disrupt the United States' healthcare and healthcare regulatory systems. Such disruptions could divert healthcare resources away from, or materially delay, FDA review and potential approval of our product candidates and new indications for our marketed products. In addition, some of our clinical trials were previously and may in the future be affected by the COVID-19 pandemic. This impact could result in further delays in site initiation and patient enrollment due to prioritization of hospital resources toward the COVID-19 pandemic, patients' inability to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, and restrictions on trial initiations imposed by hospitals and other trial sites as a result of the COVID-19 pandemic. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, was previously and may in the future be delayed or disrupted. We continue to evaluate the adverse impact of the COVID-19 pandemic on an individual trial basis. Any such disruptions may further negatively impact the progress of our clinical trials, including the readouts of trial results, the timing of regulatory review, and any anticipated program milestones.

While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, it previously caused significant disruption of global financial markets and could cause more economic disruption in the future, making it more difficult for us to access capital if needed. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our Common Stock.

To the extent the COVID-19 pandemic adversely affects our business, prospects, operating results, or financial condition, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

We face risks related to the development, manufacturing, and commercialization of REGEN-COV and "next generation" monoclonal antibodies targeting SARS-CoV-2.

In response to the COVID-19 pandemic, we developed REGEN-COV (known as Ronapreve in other countries outside the United States), a novel investigational antibody cocktail treatment designed to prevent and treat infection from the SARS-CoV-2 virus. REGEN-COV received an EUA from the FDA in November 2020 for the treatment of mild to moderate COVID-19 in certain patients. However, based on laboratory data that showed markedly decreased binding to the Omicron spike protein, REGEN-COV is highly unlikely to be active against the Omicron variant. In January 2022, the FDA revised the EUA to exclude its use in geographic regions where, based on available information including variant susceptibility and regional variant frequency, infection or exposure is likely due to a variant such as Omicron that is not susceptible to the treatment. With this EUA revision, REGEN-COV is not currently authorized for use in any U.S. states, territories, or jurisdictions, since Omicron is currently the dominant variant across the United States.

In light of these developments, we cannot predict whether (if at all) or to what extent REGEN-COV may be reauthorized for use by the FDA in any such jurisdictions in the future. In addition, there can be no assurance with respect to how long the EUA will remain in effect or whether the EUA will be further revised or revoked by the FDA based on its determination that the underlying health emergency no longer exists or warrants such authorization or other reasons. Similar limitations on the use of REGEN-COV may also be imposed by foreign regulatory authorities in jurisdictions where REGEN-COV is currently authorized for use. It is also possible that the FDA and certain other regulatory authorities may not grant REGEN-COV full marketing approval for the treatment or prevention of COVID-19, or that any such marketing approvals, if granted, may have similar or other significant limitations on its use. Further, besides currently available therapeutic and prevention options for COVID-19, additional products for treatment or prevention of COVID-19 that are more efficacious, more easily administered, more cost-effective, or otherwise

superior may be successfully developed; and utilization of REGEN-COV previously was, and any future utilization may be, adversely impacted by other factors, such as the rollout of vaccines providing acquired immunity against COVID-19, other products for treatment or prevention of COVID-19, or the distribution model for REGEN-COV. Any of these factors may further negatively impact any potential future uptake or commercialization of REGEN-COV, and such impact may be material. The intense public interest, including speculation by the media, in the development and commercialization of monoclonal antibodies and other products for treatment or prevention of COVID-19 has caused or contributed to significant volatility in our stock price, which may continue as data and other information from any studies evaluating REGEN-COV (whether conducted by us or others), our "next generation" monoclonal antibodies targeting SARS-CoV-2 discussed below, and third-party product candidates for the treatment or prevention of COVID-19 as well as any other regulatory actions become public. We are also subject to similar risks in connection with the development and potential commercialization of any such "next generation" monoclonal antibodies.

In addition to our REGEN-COV program, we are progressing "next generation" monoclonal antibodies targeting SARS-CoV-2 that are active against Omicron, Delta, and other variants of concern. Although, pending regulatory discussions, new therapeutic candidates could enter clinical development in the coming months, there can be no assurance of the timing of commencement or completion of any such future studies or favorable results from any of them.

We also face risks related to our significant investment in the development, supply, allocation, distribution, pricing, and commercialization of REGEN-COV and our "next generation" monoclonal antibodies (together with REGEN-COV referred to below as "our COVID-19 monoclonal antibodies"). Given the severity and urgency of the COVID-19 pandemic, we have committed and expect to continue to commit significant capital and resources to fund and supply clinical trials and to accelerate and scale up the production of our COVID-19 monoclonal antibodies, which involves a complex manufacturing process that is both resource- and time-sensitive. We expect our investment in the development and manufacture of our COVID-19 monoclonal antibodies to continue through 2022 and potentially beyond, although the magnitude of our investment will be subject to clinical data results, the duration of the COVID-19 pandemic, and other factors, including regulatory outcomes. If we are unable to obtain a new EUA for any of our "next generation" monoclonal antibodies, or obtain regulatory approvals for any of the foregoing, or if we make a strategic decision to discontinue development of our COVID-19 monoclonal antibodies or are otherwise not successful in their commercialization, we may be unable to recoup our significant expenses incurred to date and/or in the future related to the development and production of our COVID-19 monoclonal antibodies. While we previously recognized significant revenues in connection with sales of REGEN-COV, the degree to which future sales of our COVID-19 monoclonal antibodies will continue to impact our results of operations is highly uncertain.

In addition, our internal and contracted manufacturing capacity may not be sufficient to cover any potential future demand for our COVID-19 monoclonal antibodies. While we have entered into a collaboration agreement with Roche to develop, manufacture, and distribute outside the United States REGEN-COV, we cannot be certain that our current manufacturing and distribution capacity for REGEN-COV and the increased manufacturing and distribution capacity through our collaboration with Roche will be sufficient if there is significant future demand for REGEN-COV. In addition, we rely entirely on third parties for filling and finishing services for REGEN-COV and, in the future, may rely entirely on such providers for filling and finishing services for our other COVID-19 monoclonal antibodies. Our third-party fill/finish providers may not have sufficient capacity or may otherwise not be able to provide such services on a timely basis in the quantities requested (such as because they devote their capacity to other drugs or vaccines against COVID-19), which we previously experienced. The ability of our third-party providers to deliver such services to us may further be adversely impacted by the imposition of government restrictions or limitations (including those that may be imposed under the Defense Production Act). If we are unable to timely enter into alternative arrangements, or if such alternative arrangements are not available on satisfactory terms or at all, we may experience delays in the development, manufacturing, and distribution of our COVID-19 monoclonal antibodies.

We and Roche have faced and may in the future face additional challenges related to the allocation of supply of REGEN-COV and other COVID-19 monoclonal antibodies (as applicable), particularly with respect to geographic distribution. For example, if supplies of REGEN-COV are constrained in response to future demand, it is possible that the U.S. government may limit or restrict our and/or Roche's ability to distribute and commercialize REGEN-COV outside the United States. In addition, as a result of the emergency situations in many countries, there is a heightened risk that products for treatment or prevention of COVID-19 may be subject to adverse governmental actions in certain countries. The U.S. government may exercise or assert certain rights with respect to our inventions, products, or product candidates. For example, under the Defense Production Act, the U.S. government may, among other things, require domestic industries to provide essential goods and services needed for the national defense, such as drug material or other supplies needed to treat COVID-19 patients, which could require us to allocate manufacturing capacity in a way that impacts our regular operations. In addition, our agreements with the U.S. government contain provisions granting the U.S. government certain rights relating to products, product candidates, and related inventions (as applicable) covered by those agreements. For example, our July 2020 agreement with the U.S. government to manufacture and deliver REGEN-COV to the U.S. government gives the U.S. government, among other rights, the right to require us to grant a non-exclusive license to applicable inventions to a third party if such action is deemed necessary to alleviate certain health or safety needs. This right may be triggered if we, for example, do not manufacture or supply sufficient product to address such

needs. If the U.S. government exercises or asserts any such rights or imposes these or similar measures with respect to our products, product candidates, or related inventions (including our COVID-19 monoclonal antibodies), it may adversely impact our business and results of operations. Foreign governments (including the government of Ireland, where we have manufacturing facilities) may have similar rights or attempt to assert any such rights. Further, we have observed and are likely to continue to face significant public attention and scrutiny over the complex decisions made regarding the development program for our COVID-19 monoclonal antibodies, including any allocation, distribution, or pricing decisions. If we are unable to successfully manage these risks, we could face significant reputational harm, which could, among other adverse consequences, negatively affect our stock price.

Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products

We are substantially dependent on the success of EYLEA and Dupixent.

EYLEA net sales represent a substantial portion of our revenues and this concentration of our net sales in a single product makes us substantially dependent on that product. For the years ended December 31, 2021 and 2020, EYLEA net sales in the United States represented 36% and 58% of our total revenues, respectively, with EYLEA net sales as a percentage of our total revenues for the year ended December 31, 2021 being significantly lower due to the net product sales of REGEN-COV we recorded in that period in connection with deliveries of drug product under our agreements with the U.S. government. If we were to experience difficulty with the commercialization of EYLEA in the United States or if Bayer were to experience any difficulty with the commercialization of EYLEA outside the United States (including as a result of the COVID-19 pandemic discussed above), or if we and Bayer are unable to maintain current marketing approvals of EYLEA, we may experience a reduction in revenue and may not be able to sustain profitability, and our business, prospects, operating results, and financial condition would be materially harmed.

In addition, we are dependent on our share of profits from the commercialization of Dupixent under our Antibody Collaboration with Sanofi. If we or Sanofi were to experience any difficulty with the commercialization of Dupixent or if we or Sanofi are unable to maintain current marketing approvals of Dupixent, we may experience a reduction in revenue and our business, prospects, operating results, and financial condition would be materially harmed.

If we or our collaborators are unable to continue to successfully commercialize our products, our business, prospects, operating results, and financial condition will be materially harmed.

We expect that the degree of commercial success of our marketed products will continue to depend on many factors, including the following (as applicable):

- the continued impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on our business and the demand for our marketed products, as well as its continued impact on, among other things, our employees, collaborators, suppliers, and other third parties on which we rely, our ability to continue to manage our supply chain, and the global economy (as further discussed above under "Risks Related to the COVID-19 Pandemic - *Our business may be further adversely affected by the effects of the COVID-19 pandemic*");
- effectiveness of the commercial strategy in and outside the United States for the marketing of our products, including pricing strategy;
- sufficient coverage of, and reimbursement for, our marketed products by third-party payors, including Medicare and Medicaid in the United States and other government and private payors in the United States and foreign jurisdictions, as well as U.S. and foreign payor restrictions on eligible patient populations and the reimbursement process (including drug price control measures that have been or may be introduced in the United States by various federal and state authorities);
- our ability and our collaborators' ability to maintain sales of our marketed products in the face of competitive products and to differentiate our marketed products from competitive products, including as applicable product candidates currently in clinical development; and, in the case of EYLEA, the existing and potential new branded and biosimilar competition for EYLEA (discussed further under "*The commercial success of our products and product candidates is subject to significant competition* - Marketed Products" below) and the willingness of retinal specialists and patients to start or continue treatment with EYLEA or to switch from another product to EYLEA;
- the effect of existing and new health care laws and regulations currently being considered or implemented in the United States, including price reporting and other disclosure requirements of such laws and regulations and the potential impact of such requirements on physician prescribing practices and payor coverage;
- serious complications or side effects in connection with the use of our marketed products, as discussed under "Risks Related to Maintaining Approval of Our Marketed Products and the Development and Obtaining Approval of Our Product Candidates and New Indications for Our Marketed Products - *Serious complications or side effects in connection with the use of our products and in clinical trials for our product candidates and new indications for our marketed products could cause our regulatory approvals to be revoked or limited or lead to delay or discontinuation of*

development of our product candidates or new indications for our marketed products, which could severely harm our business, prospects, operating results, and financial condition" below;
- maintaining and successfully monitoring commercial manufacturing arrangements for our marketed products with third parties who perform fill/finish or other steps in the manufacture of such products to ensure that they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities;
- our ability to meet the demand for commercial supplies of our marketed products;
- the outcome of the pending proceedings relating to EYLEA, Dupixent, Praluent, and REGEN-COV (described further in Note 15 to our Consolidated Financial Statements included in this report), as well as other risks relating to our marketed products and product candidates associated with intellectual property of other parties and pending or future litigation relating thereto (as discussed under "Risks Related to Intellectual Property and Market Exclusivity" below);
- the outcome of the pending government proceedings and investigations and other matters described in Note 15 to our Consolidated Financial Statements included in this report (including the civil complaint filed against us on June 24, 2020 in the U.S. District Court for the District of Massachusetts by the U.S. Attorney's Office for the District of Massachusetts); and
- the results of post-approval studies, whether conducted by us or by others and whether mandated by regulatory agencies or voluntary, and studies of other products that could implicate an entire class of products or are perceived to do so.

More detailed information about the risks related to the commercialization of our marketed products is provided in the risk factors below.

We and our collaborators are subject to significant ongoing regulatory obligations and oversight with respect to the products we or our collaborators commercialize. If we or our collaborators fail to maintain regulatory compliance for any of such products, the applicable marketing approval may be withdrawn, which would materially harm our business, prospects, operating results, and financial condition.

We and our collaborators are subject to significant ongoing regulatory obligations and oversight with respect to the products we or they commercialize for the products' currently approved indications in the United States, EU, and other countries where such products are approved. If we or our collaborators fail to maintain regulatory compliance or satisfy other obligations for such products' currently approved indications (including because the product does not meet the relevant endpoints of any required post-approval studies (such as those required under an accelerated approval by the FDA or other similar type of approval), or for any of the reasons discussed below under "Risks Related to Maintaining Approval of Our Marketed Products and the Development and Obtaining Approval of Our Product Candidates and New Indications for Our Marketed Products - *Obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain*"), the applicable marketing approval may be withdrawn, which would materially harm our business, prospects, operating results, and financial condition. Failure to comply may also subject us to sanctions, product recalls, or withdrawals of previously approved marketing applications. See also "Risks Related to Manufacturing and Supply - *Our or our collaborators' failure to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates could result in incurring substantial remedial costs, delays in the development or approval of our product candidates or new indications for our marketed products and/or in their commercial launch if regulatory approval is obtained, and a reduction in sales*" below.

Sales of our marketed products are dependent on the availability and extent of reimbursement from third-party payors, and changes to such reimbursement may materially harm our business, prospects, operating results, and financial condition.

Sales of our marketed products in the United States are dependent, in large part, on the availability and extent of reimbursement from third-party payors, including private payor healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies ("PBMs"), and government programs such as Medicare and Medicaid. Sales of our marketed products in other countries are dependent, in large part, on similar reimbursement mechanisms and programs in those countries.

Our future revenues and profitability will be adversely affected in a material manner if such third-party payors do not adequately defray or reimburse the cost of our marketed products to patients. If these entities do not provide coverage and reimbursement with respect to our marketed products or provide an insufficient level of coverage and reimbursement, such products may be too costly for many patients to afford them, and physicians may not prescribe them. Many third-party payors cover only selected drugs, or may prefer selected drugs, making drugs that are not covered or preferred by such payors more expensive for patients. Third-party payors may also require prior authorization for reimbursement, or require failure on another type of treatment before covering a particular drug, particularly with respect to higher-priced drugs. As our currently marketed products and most of our product candidates are biologics, bringing them to market may cost more than bringing traditional, small-molecule drugs to market due to the complexity associated with the research, development, production, supply, and regulatory review of such products. Given cost sensitivities in many health care systems (which will likely be exacerbated as a result of the COVID-19

pandemic), our currently marketed products and product candidates are likely to be subject to continued pricing pressures, which may have an adverse impact on our business, prospects, operating results, and financial condition.

In addition, in order for private insurance and governmental payors (such as Medicare and Medicaid in the United States) to reimburse the cost of our marketed products, we must maintain, among other things, our FDA registration and our National Drug Code, formulary approval by PBMs, and recognition by insurance companies and CMS. There is no certainty that we will be able to obtain or maintain the applicable requirements for reimbursement (including relevant formulary coverage, as discussed further below) of our current and future marketed products, which may have a material adverse effect on our business.

Government and other third-party payors (including PBMs) are challenging the prices charged for healthcare products and increasingly limiting, and attempting to limit, both coverage and level of reimbursement for prescription drugs, such as by requiring outcomes-based or other pay-for-performance pricing arrangements. They are also imposing restrictions on eligible patient populations and the reimbursement process, including by means of required prior authorizations and utilization management criteria, such as step therapy (i.e., requiring the use of less costly medications before more costly medications are approved for coverage). Some states are also considering legislation that would control the prices and reimbursement of prescription drugs, and state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any prescription drug for which supplemental rebates are not being paid. It is likely that federal and state legislatures and health agencies will continue to focus on additional health care reform measures in the future that will impose additional constraints on prices and reimbursements for our marketed products; this trend may be further accelerated as a result of the COVID-19 pandemic.

Further, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation and policies (in addition to those already in effect) designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the out-of-pocket cost of prescription drugs, and reform government program reimbursement methodologies for drugs. President Biden and various members of his administration and the current U.S. Congress have indicated that lowering drug prices continues to be a legislative and political priority, as evidenced, for example, by the "Executive Order on Promoting Competition in the American Economy" issued by President Biden in July 2021. The main proposal aimed at drug pricing introduced at the federal level as part of the "Build Back Better Act" includes measures that would allow the government to negotiate prices of certain prescription drugs under Medicare (including those covered under Medicare Part B, such as EYLEA) and would redesign the Medicare Part D benefit to limit patient out-of-pocket drug costs and shift liabilities among stakeholders, including manufacturers. At the state level, legislatures are becoming increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and price and marketing cost disclosure and transparency measures. In some cases, these measures are designed to encourage importation from other countries and bulk purchasing. A reduction in the availability or extent of reimbursement from U.S. government programs (including as a result of the proposals, initiatives, and developments described above) could have a material adverse effect on the sales of EYLEA or our other marketed products. Economic pressure on state budgets may also have a similar impact.

In addition, PBMs often develop formularies to reduce their cost for medications. The breadth of the products covered by formularies varies considerably from one PBM to another. Failure to be included in such formularies or to achieve favorable formulary status may negatively impact the utilization and market share of our marketed products. If our marketed products are not included within an adequate number of formularies, adequate reimbursement levels are not provided, the eligible insured patient population for our products is limited, or a key payor refuses to provide reimbursement for our products in a particular jurisdiction altogether, this could have a material adverse effect on our and our collaborators' ability to commercialize the applicable product.

In certain foreign countries, pricing, coverage, and level of reimbursement of prescription drugs are subject to governmental control, and we and our collaborators may be unable to obtain coverage, pricing, and/or reimbursement on terms that are favorable to us or necessary for us or our collaborators to successfully commercialize our marketed products in those countries. In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country, and may take into account the clinical effectiveness, cost, and service impact of existing, new, and emerging drugs and treatments. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Our results of operations may suffer if we or our collaborators are unable to market our products in foreign countries or if coverage and reimbursement for our marketed products in foreign countries is limited or delayed.

The commercial success of our products and product candidates is subject to significant competition.

Marketed Products

There is substantial competition in the biotechnology and pharmaceutical industries from biotechnology, pharmaceutical, and chemical companies. Many of our competitors have substantially greater research, preclinical and clinical product development and manufacturing capabilities, as well as financial, marketing, and human resources, than we do. Our competitors, regardless of their size, may also enhance their competitive position if they acquire or discover patentable inventions, form collaborative arrangements, or merge with other pharmaceutical or biotechnology companies. There is significant actual and potential future competition for each of our marketed products.

EYLEA faces significant competition in the marketplace. For example, EYLEA competes in one or more of its approved indications with other VEGF inhibitors, including Novartis and Genentech/Roche's Lucentis, Novartis' Beovu, and Genentech/Roche's Susvimo, as well as Samsung Bioepis and Biogen's biosimilar referencing Lucentis. In addition, Genentech/Roche recently announced the approval of Vabysmo™ (faricimab-svoa), a bispecific antibody targeting both VEGF and Ang2, for the treatment of wet AMD and DME in the United States. Ophthalmologists are also using off-label, third-party repackaged versions of Genentech/Roche's approved VEGF antagonist, bevacizumab, for the treatment of certain of EYLEA's indications, and we are aware of another company developing an ophthalmic formulation of such product. In DME and RVO, EYLEA also competes with intravitreal implants of corticosteroids. We are also aware of a number of companies working on the development of product candidates and extended delivery devices for the potential treatment of one or more of EYLEA's indications, including those that act by blocking VEGF and VEGF receptors (including therapies designed to extend the treatment interval) and/or other targets. In addition, we are aware of several companies developing biosimilar versions of EYLEA and other approved anti-VEGF treatments. Other potentially competitive products in development include products for use in combination with EYLEA and/or other anti-VEGF treatments, small-molecule tyrosine kinase inhibitors, gene therapies, and other eye-drop formulations, devices, and oral therapies. There also is a risk that third parties repackage ZALTRAP for off-label use and sale for the treatment of diseases of the eye, even though ZALTRAP has not been manufactured and formulated for use in intravitreal injections. We are aware of claims by third parties, including those based on published clinical data, alleging that ZALTRAP may be safely administered to the eye.

The market for Dupixent's current and potential future indications is also increasingly competitive. In atopic dermatitis, there are several topical ointments or agents either approved or in development. There are also topical and systemic JAK inhibitors and an antibody against IL-13 approved for atopic dermatitis and others are in development. In addition, a number of companies are developing antibodies against IL-13Ra1, OX40, IL-31R, and/or IL-1alpha. In asthma, competitors to Dupixent include antibodies against the IL-5 ligand or the IL-5 receptor, immunoglobulin E, or thymic stromal lymphopoietin ("TSLP"); and some of these antibodies are either approved or in development for indications that also compete or may compete in the future with Dupixent in CRSwNP. There are several other potentially competitive products in development that may compete with Dupixent in asthma, as well as potential future indications, including antibodies against the IL-33 ligand or receptor. Dupixent also faces competition from inhaled products in asthma and potential future indications.

Libtayo also faces significant competition. There are several competitors that are marketing and/or developing antibodies against PD-1 and/or PDL-1 (some of which were approved in the relevant indications and commercialized before Libtayo), including Merck's Keytruda, Bristol-Myers Squibb's Opdivo, Roche's Tecentriq, and AstraZeneca's Imfinzi.

There is also significant actual and potential future competition for other products marketed or otherwise commercialized by us and/or our collaborators under our collaboration agreements with them. For example, there are several companies that are marketing and/or developing antibodies or other molecules (such as small interfering RNA molecules, or siRNAs) against PCSK9, ANGPTL3 and IL-6 and/or IL-6R, which currently (or, for product candidates in development, may in the future if approved) compete with Praluent, Evkeeza, and Kevzara, respectively.

Product Candidates

Our *VelocImmune* technology, other antibody generation technologies, and late-stage and earlier-stage clinical candidates face competition from many pharmaceutical and biotechnology companies using various technologies, including antibody generation technologies and other approaches such as RNAi, chimeric antigen receptor T cell (CAR-T cell), and gene therapy technologies. For example, we are aware of other pharmaceutical and biotechnology companies actively engaged in the research and development of antibody-based products against targets that are also the targets of our early- and late-stage product candidates. We are also aware of other companies developing or marketing small molecules or other treatments that may compete with our antibody-based product candidates in various indications, if such product candidates obtain regulatory approval in those indications. If any of these or other competitors announces a successful clinical study involving a product that may be competitive with one of our product candidates or the grant of marketing approval by a regulatory agency for a competitive product, such developments may have an adverse effect on our business or future prospects. In addition, the first product to reach the market in

a therapeutic area is often at a significant competitive advantage relative to later entrants to the market. Accordingly, the relative speed with which we, or our collaborators, can develop our product candidates, complete the clinical trials and approval processes, and, if such product candidates are approved for marketing and sale, supply commercial quantities to the market is expected to continue to be an important competitive factor. Due to the uncertainties associated with developing biopharmaceutical products, we may not be the first to obtain marketing approval for a product against any particular target, which may have a material adverse effect on our business or future prospects.

We rely on our collaborations with Bayer and Sanofi for commercializing some of our marketed products.

While we have established our own sales and marketing organization for EYLEA in the United States for its currently approved indications, we have no sales, marketing, commercial, or distribution capabilities for EYLEA outside the United States. Under the terms of our license and collaboration agreement with Bayer (which is terminable by Bayer at any time upon six or twelve months' advance notice, depending on the circumstances giving rise to termination), we rely on Bayer (and, in Japan, Santen pursuant to a Co-Promotion and Distribution Agreement with Bayer's Japanese affiliate, as in effect from time to time) for sales, marketing, and distribution of EYLEA in countries outside the United States.

In addition, under the terms of our Antibody Collaboration and our IO Collaboration, we and Sanofi co-commercialize Dupixent and Libtayo in the United States. As a result, we rely in part on Sanofi's sales and marketing organization in the United States for these products. If we and Sanofi fail to coordinate our United States sales and marketing efforts effectively, sales of any of such products may be materially affected. Sanofi also maintains other important responsibilities relating to Dupixent in the United States. For example, Sanofi records product sales for Dupixent in the United States and leads negotiations with payors relating to this product. We also rely on Sanofi for sales, marketing, and distribution of Dupixent and Libtayo in countries outside the United States. While we exercised our option under the Antibody Collaboration to co-commercialize Dupixent in certain jurisdictions outside the United States and have commenced this co-commercialization, we will continue to rely in part on Sanofi's sales and marketing organization in such jurisdictions and there can be no assurance that we will be able to successfully conduct such co-commercialization in the expected time frame or at all.

If we and our collaborators are unsuccessful in continuing to commercialize the marketed products subject to such collaborations, or if Bayer or Sanofi terminate their respective collaborations with us, our business, prospects, operating results, and financial condition would be materially impaired. We have limited commercial capabilities outside the United States and would have to develop or outsource these capabilities. Therefore, termination of the Bayer collaboration agreement, our Antibody Collaboration, or our IO Collaboration would create substantial new and additional risks to the successful commercialization of the applicable products, particularly outside the United States. For additional information regarding our collaborations with Bayer and Sanofi, see "Risks Related to Our Reliance on Third Parties - *If our collaboration with Bayer for EYLEA is terminated, or Bayer materially breaches its obligations thereunder, our business, prospects, operating results, and financial condition, and our ability to continue to develop EYLEA and commercialize EYLEA outside the United States in the time expected, or at all, would be materially harmed*" below and "Risks Related to Our Reliance on Third Parties - *If our Antibody Collaboration or our IO Collaboration with Sanofi is terminated, or Sanofi materially breaches its obligations thereunder, our business, prospects, operating results, and financial condition, and our ability to develop, manufacture, and commercialize certain of our products and product candidates in the time expected, or at all, would be materially harmed*" below.

Sales of our marketed products recorded by us and our collaborators could be reduced by imports from countries where such products may be available at lower prices.

Our sales of products we commercialize in the United States and our collaborators' sales of products they commercialize or co-commercialize with us under our collaboration agreements with them in the United States and other countries (which impact our share of any profits or losses from the commercialization of these products under the relevant collaboration agreements and, therefore, our results of operations) may be reduced if the applicable product is imported into those countries from lower priced markets, whether legally or illegally (a practice known as parallel trading or reimportation). Parallel traders (who may repackage or otherwise alter the original product or sell it through alternative channels such as mail order or the Internet) take advantage of the price differentials between markets arising from factors including sales costs, market conditions (such as intermediate trading stages), tax rates, or national regulation of prices. Under our arrangement with Bayer, pricing and reimbursement for EYLEA outside the United States is the responsibility of Bayer. Similarly, under our Antibody Collaboration and IO Collaboration with Sanofi, pricing and reimbursement for the products commercialized or co-commercialized thereunder outside the United States are the responsibility of Sanofi. Prices for our marketed products in jurisdictions outside the United States are based on local market economics and competition and are likely to differ from country to country. In the United States, prices for pharmaceuticals are generally higher than in the bordering nations of Canada and Mexico and sales of our marketed products in the United States may be reduced if the applicable product marketed in those bordering nations is imported into the United States. In addition, there are proposals to legalize the import of pharmaceuticals from outside the United States into the United States. If such proposals were implemented, our future revenues derived from sales of our marketed products could be reduced. Parallel-

trading practices also are of particular relevance to the EU, where they have been encouraged by the current regulatory framework. These types of imports may exert pressure on the pricing of our marketed products in a particular market or reduce sales recorded by us or our collaborators, thereby adversely affecting our results of operations.

We may be unsuccessful in continuing the commercialization of our marketed products or in commercializing our product candidates or new indications for our marketed products, if approved, which would materially and adversely affect our business, profitability, and future prospects.

Even if clinical trials demonstrate the safety and effectiveness of any of our product candidates for a specific disease and the necessary regulatory approvals are obtained, the commercial success of any of our product candidates or new indications for our marketed products will depend upon, among other things, their acceptance by patients, the medical community, and third-party payors and on our and our collaborators' ability to successfully manufacture, market, and distribute those products in substantial commercial quantities or to establish and manage the required infrastructure to do so, including large-scale information technology systems and a large-scale distribution network. Establishing and maintaining sales, marketing, and distribution capabilities are expensive and time-consuming. Even if we obtain regulatory approval for our product candidates or new indications, if they are not successfully commercialized, we will not be able to recover the significant investment we have made in developing such products and our business, prospects, operating results, and financial condition would be severely harmed.

The commercial success of our products may also be adversely affected by guidelines or recommendations to healthcare providers, administrators, payors, and patient communities that result in decreased use of our products. Such guidelines or recommendations may be published not only by governmental agencies, but also professional societies, practice management groups, private foundations, and other interested parties.

Our product candidates are delivered either by intravenous infusion or by intravitreal or subcutaneous injections, which are generally less well received by patients than tablet or capsule delivery and this could adversely affect the commercial success of those products if they receive marketing approval.

We are dependent upon a small number of customers for a significant portion of our revenue, and the loss of or significant reduction in sales to these customers would adversely affect our results of operations.

We sell our marketed products for which we record net product sales in the United States to several distributors and specialty pharmacies, as applicable, which generally sell the product directly to healthcare providers or other pharmacies (as applicable). For the years ended December 31, 2021 and 2020, our gross product sales of such products to two customers accounted on a combined basis for 48% and 83% of our total gross product revenue, respectively, and gross product sales of REGEN-COV to the U.S. government accounted for an additional 43% of our gross product revenue for the year ended December 31, 2021. We expect significant customer concentration to continue for the foreseeable future, although the degree to which future sales of REGEN-COV will continue to impact our results of operations is highly uncertain. Our ability to generate and grow sales of these products will depend, in part, on the extent to which our distributors and specialty pharmacies are able to provide adequate distribution of these products to healthcare providers. Although we believe we can find additional distributors, if necessary, our revenue during any period of disruption could suffer and we might incur additional costs. In addition, these customers are responsible for a significant portion of our net trade accounts receivable balances. The loss of any large customer, a significant reduction in sales we make to them, any cancellation of orders they have made with us, or any failure to pay for the products we have shipped to them could adversely affect our results of operations.

If we are unable to establish commercial capabilities outside the United States for products we intend to commercialize or co-commercialize outside the United States, our business, prospects, operating results, and financial condition may be adversely affected.

We have limited commercial capabilities outside the United States and do not currently have a fully established organization for the sales, marketing, and distribution of marketed products outside the United States. We will need to establish commercial capabilities outside the United States for any new product we decide to commercialize or co-commercialize outside the United States. For example, following the exercise of our option under the Antibody Collaboration to co-commercialize Dupixent in certain jurisdictions outside the United States, we have begun establishing commercial capabilities for Dupixent in such jurisdictions. There may be other circumstances in which we need to establish commercial capabilities outside the United States, including because we decide to commercialize a particular product independently; we are unable to find an appropriate collaborator; or our existing collaborator decides not to opt in, decides to opt out, or breaches its obligations to us with respect to a particular product.

In order to commercialize or co-commercialize any products outside the United States, we must build our sales, marketing, distribution, managerial, and other non-technical capabilities in the relevant markets or make arrangements with third parties to perform these services, any of which will likely be expensive and time consuming and could delay product launch or the co-

commercialization of a product in one or more markets outside the United States. We cannot be certain that we will be able to successfully develop commercial capabilities outside the United States (including as it relates to Dupixent) within an acceptable time frame, without incurring substantial expenses, or at all. These and other difficulties relating to commercializing our products outside the United States may severely harm our business, prospects, operating results, and financial condition.

Risks Related to Maintaining Approval of Our Marketed Products and the Development and Obtaining Approval of Our Product Candidates and New Indications for Our Marketed Products

If we or our collaborators do not maintain regulatory approval for our marketed products, and obtain regulatory approval for our product candidates or new indications for our marketed products, we will not be able to market or sell them, which would materially and negatively impact our business, prospects, operating results, and financial condition.

We cannot sell or market products without regulatory approval. If we or our collaborators do not maintain regulatory approval for our marketed products, and obtain regulatory approval for our product candidates or new indications of our marketed products (or are materially delayed in doing so), the value of our Company and our business, prospects, operating results, and financial condition may be materially harmed.

Obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain.

In the United States, we (which, for purposes of this risk factor, includes our collaborators, unless otherwise stated or required by the context) must obtain and maintain approval from the FDA for each drug we intend to sell. Obtaining FDA approval is typically a lengthy and expensive process, and approval is highly uncertain. We cannot predict with certainty if or when we might submit for regulatory approval for any of our product candidates currently under development. Any approvals we may obtain may not cover all of the clinical indications for which we are seeking approval. Also, an approval might contain significant limitations in the form of narrow indications, warnings, precautions, or contra-indications with respect to conditions of use. Additionally, the FDA may determine that a REMS is necessary to ensure that the benefits of a new product outweigh its risks, and the product can therefore be approved. A REMS may include various elements, ranging from a medication guide or patient package insert to limitations on who may prescribe or dispense the drug, depending on what the FDA considers necessary for the safe use of the drug. The FDA has substantial discretion in the approval process (including with respect to setting specific conditions for submission) and may either refuse to accept an application for substantive review or may form the opinion after review of an application that the application is insufficient to allow approval of a product candidate. If the FDA does not accept our application for review or approve our application, it may require that we conduct additional clinical, preclinical, or manufacturing validation studies and submit the data before it will reconsider our application. Depending on the extent of these or any other studies that might be required, approval of any applications that we submit may be delayed significantly, or we may be required to expend more resources. It is also possible that any such additional studies, if performed and completed, may not be considered sufficient by the FDA to make our applications approvable. If any of these outcomes occur, we may be forced to delay or abandon our applications for approval.

In certain instances (such as when we use a biomarker-based test to identify and enroll specific patients in a clinical trial), regulatory approval of a companion diagnostic to our therapeutic product candidate may be required as a condition to regulatory approval of the therapeutic product candidate. We may need to rely on third parties to provide companion diagnostics for use with our product candidates. Such third parties may be unable or unwilling on terms acceptable to us to provide such companion diagnostics or to obtain timely regulatory approval of such companion diagnostics, which could negatively impact regulatory approval of our product candidates or may result in increased development costs or delays.

The FDA may also require us to conduct additional clinical trials after granting approval of a product. Its ability to do so has been enhanced by the Food and Drug Administration Amendments Act of 2007, pursuant to which the FDA has the explicit authority to require postmarketing studies (also referred to as post-approval or Phase 4 studies), labeling changes based on new safety information, and compliance with FDA-approved risk evaluation and mitigation strategies. Post-approval studies, whether conducted by us or by others and whether mandated by regulatory agencies or voluntary, and other data about our marketed products (or data about products similar to our marketed products that implicate an entire class of products or are perceived to do so) may result in changes in product labeling, restrictions on use, product withdrawal or recall, loss of approval, or lower sales of our products. Obligations equivalent in scope, but which can vary widely in application, apply in foreign countries.

According to the FDA policies under the Prescription Drug User Fee Act, the FDA system of review times for new drugs includes standard review and priority review. The FDA's goal for a standard review is to review the application within a 10-month time frame from the time the application is filed by the FDA (filing date), which typically occurs approximately 60 days following submission of the application by the applicant. The FDA has stated the goal to act on 90% of standard new molecular entity ("NME") New Drug Application ("NDA") and original BLA submissions within 10 months of the filing date. A priority review designation is given to drugs that treat a serious condition and offer major advances in treatment, or provide a treatment where no adequate therapy exists, and may also be afforded to a human drug application based on a priority review voucher. The FDA has

stated the goal to act on 90% of priority NME NDA and original BLA submissions within six months of the filing date. However, the FDA's review goals are subject to change and the duration of the FDA's review depends on a number of factors, including the number and types of other applications that are submitted to the FDA around the same time period or are pending. Even if any of our applications receives a priority review designation, we may not ultimately be able to obtain approval of our application within a time frame consistent with the FDA's stated review goals or at all, and such designation may not actually lead to a faster development or regulatory review or approval process. Procedures that are equivalent in scope, but which can vary widely in application, apply in foreign countries.

The FDA and comparable foreign regulatory authorities enforce GCPs and other regulations and legal requirements through periodic inspections of trial sponsors, clinical research organizations ("CROs"), principal investigators, and trial sites. If we or any of the third parties conducting our clinical studies are determined to have failed to fully comply with GCPs, the study protocol or applicable regulations, the clinical data generated in those studies may be deemed unreliable. This and similar instances of non-compliance with GCPs could result in non-approval of our product candidates by the FDA or foreign regulatory authorities such as the EC, or we or the FDA or such other regulatory authorities may decide to conduct additional inspections or require additional clinical studies, which would delay our development programs, require us to incur additional costs, and could substantially harm our business, prospects, operating results, and financial condition.

Before approving a new drug or biologic product, the FDA and such comparable foreign regulatory authorities require that the facilities at which the product will be manufactured or advanced through the supply chain be in compliance with current Good Manufacturing Practices, or cGMP, requirements and regulations governing the manufacture, shipment, and storage of the product. Additionally, manufacturers of biological products and their facilities are subject to payment of substantial user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and adherence to any commitments made in the applicable BLA. These cGMP requirements and regulations are not prescriptive instructions on how to manufacture products, but rather a series of principles that must be observed during manufacturing; as a result, their implementation may not be clearly delineated and may present a challenging task. Manufacturing product candidates in compliance with these regulatory requirements is complex, time-consuming, and expensive. To be successful, our products must be manufactured in compliance with regulatory requirements, and at competitive costs. If we or any of our third-party manufacturers, product packagers, labelers, or other parties performing steps in the supply chain are unable to maintain regulatory compliance with cGMP, the FDA and comparable foreign regulatory authorities can impose monetary penalties or other civil or criminal sanctions, including, among other things, refusal to approve a pending application for a new drug or biologic product, or revocation of a pre-existing approval. For additional information, see "Risks Related to Manufacturing and Supply - *Our or our collaborators' failure to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates could result in incurring substantial remedial costs, delays in the development or approval of our product candidates or new indications for our marketed products and/or in their commercial launch if regulatory approval is obtained, and a reduction in sales*." Our business, prospects, operating results, and financial condition may be materially harmed as a result of noncompliance with the requirements and regulations described in this paragraph.

We are also subject to ongoing requirements imposed by the FDA and comparable foreign regulatory authorities governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping, and reporting of safety and other post-marketing information. The holder of an approved BLA or foreign equivalent is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA or foreign equivalent must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. Advertising and promotional materials must comply with FDA regulations and those of foreign regulatory authorities and may be subject to other potentially applicable federal and state laws. The applicable regulations in countries outside the U.S. grant similar powers to the competent authorities and impose similar obligations on companies.

In addition to the standard drug approval process, the Secretary of HHS may authorize the issuance of, and the FDA Commissioner may issue, an EUA to allow an unapproved medical product to be used in an emergency based on criteria established by the Food, Drug, and Cosmetic Act, including that the product at issue may be effective in diagnosing, treating, or preventing serious or life-threatening diseases when there are no adequate, approved, and available alternatives. For example, REGEN-COV has been authorized for use in certain individuals in the United States based on an EUA from the FDA. An EUA terminates when the emergency determination underlying the EUA terminates. The FDA may also revoke, revise, or restrict an EUA for a variety of reasons, including where it is determined that the underlying health emergency no longer exists or warrants such authorization or the medical product is no longer effective in diagnosing, treating, or preventing the underlying health emergency. For example, in January 2022, the FDA revised the EUA for REGEN-COV to exclude its use in geographic regions where, based on available information including variant susceptibility and regional variant frequency, infection or exposure is likely due to a variant such as Omicron that is not susceptible to the treatment. With this EUA revision, REGEN-COV is not currently authorized for use in any U.S. states, territories, or jurisdictions, since Omicron is currently the dominant variant across the United States. Any such termination, revocation, or revision of an EUA could adversely impact our business in a variety of

ways, including by having to absorb related manufacturing and overhead costs as well as potential inventory write-offs if regulatory approval is not obtained timely or at all. For example, during the fourth quarter of 2021, we recorded a charge of $231.7 million to write down REGEN-COV inventory, as described in Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Results of Operations."

In addition to the FDA and other regulatory agency regulations in the United States, we are subject to a variety of foreign regulatory requirements governing human clinical trials, manufacturing, marketing and approval of drugs, and commercial sale and distribution of drugs in foreign countries. The foreign regulatory approval process is similarly a lengthy and expensive process, the result of which is highly uncertain, and foreign regulatory requirements include all of the risks associated with FDA approval as well as country specific regulations. We and our collaborators must maintain regulatory compliance for the products we or they commercialize in foreign jurisdictions. From time to time, we may hold a product's marketing approval in a jurisdiction outside the United States where we may have less experience and where our regulatory capabilities may be more limited. In addition, actions by a regulatory agency in a country or region with respect to a product candidate may have an impact on the approval process for that product candidate in another country or region. Foreign regulatory authorities may ask for additional data in order to begin a clinical study, including phase 3 clinical trials required to submit a MAA in the EU. In addition such authorities often have the authority to require post-approval studies, such as a PASS and/or PAES, which involve various risks similar to those described above. Whether or not we obtain FDA approval for a product in the United States, we must obtain approval of the product by the comparable regulatory authorities in foreign countries before we can market that product or any other product in those countries.

Furthermore, in the EEA, if we do not manage to retain a QPPV, to maintain a PSMF, or to comply with other pharmacovigilance obligations, we may be at risk of our clinical trials being closed prematurely, our marketing authorization being suspended, and we may be subject to other enforcement actions by the national competent authorities of the EEA or the EC.

The exact requirements concerning pharmacovigilance reporting may differ in the numerous countries in which we conduct clinical trials. Failure to comply with the related pharmacovigilance requirements may result in the premature closure of the clinical trials and other enforcement actions by the relevant regulatory authorities.

Preclinical and clinical studies required for our product candidates and new indications of our marketed products are expensive and time-consuming, and their outcome is highly uncertain. If any such studies are delayed or yield unfavorable results, regulatory approval for our product candidates or new indications of our marketed products may be delayed or become unobtainable.

As described above, we must conduct extensive testing of our product candidates and new indications of our marketed products before we can obtain regulatory approval to market and sell them. We need to conduct both preclinical animal testing and human clinical trials. Conducting such studies is a lengthy, time-consuming, and expensive process. These tests and trials may not achieve favorable results for many reasons, including, among others, failure of the product candidate to demonstrate safety or efficacy, the development of serious or life-threatening adverse events (or side effects) caused by or connected with exposure to the product candidate (or prior or concurrent exposure to other products or product candidates), difficulty in enrolling and maintaining subjects in a clinical trial, clinical trial design that may not make it possible to enroll or retain a sufficient number of patients to achieve a statistically significant result or the desired level of statistical significance for the endpoint in question, lack of sufficient supplies of the product candidate or comparator drug, and the failure of clinical investigators, trial monitors, contractors, consultants, or trial subjects to comply with the trial plan, protocol, or applicable regulations related to the FDA's GLPs or GCPs. A clinical trial may also fail because the dose(s) of the investigational drug included in the trial were either too low or too high to determine the optimal effect of the investigational drug in the disease setting.

We will need to reevaluate any drug candidate that does not test favorably and either conduct new studies, which are expensive and time consuming, or abandon that drug development program. If preclinical testing yields unfavorable results, product candidates may not advance to clinical trials. The failure of clinical trials to demonstrate the safety and effectiveness of our clinical candidates for the desired indication(s) would preclude the successful development of those candidates for such indication(s), in which event our business, prospects, operating results, and financial condition may be materially harmed.

Furthermore, some of our products and product candidates (such as Libtayo and Dupixent) are studied in combination with agents and treatments developed by us or our collaborators. There may be additional risks and unforeseen safety issues resulting from such combined administration, any of which may materially adversely impact clinical development of these product candidates and our ability to obtain regulatory approval.

In some jurisdictions such as the EU, initiating phase 3 clinical trials and clinical trials in the pediatric population is subject to a requirement to obtain approval or a waiver from the competent authorities of the EU Member States and/or the EMA. If we do not obtain such approval, our ability to conduct clinical trials and obtain marketing authorizations or approvals may be severely impaired and our business may be adversely impacted.

Certain of our research and development activities are conducted at our existing facilities primarily located in Tarrytown, New York. As we continue to expand, we may lease, operate, purchase, or construct additional facilities to expand our research and development capabilities in the future. Expanding our research and laboratory facilities may require significant time and resources. Further, we may be unable to pursue our research and development efforts if the relevant facility were to cease operations due to fire, climate change, natural disasters, acts of war or terrorism, or other disruptions. Any related delays may interfere with our research and development efforts and our business may be adversely impacted.

Successful development of our current and future product candidates is uncertain.

Only a small minority of all research and development programs ultimately result in commercially successful drugs. Clinical trials may not demonstrate statistically sufficient effectiveness and safety to obtain the requisite regulatory approvals for these product candidates in these indications. Many companies in the biopharmaceutical industry, including our Company, have suffered significant setbacks in clinical trials, even after promising results had been obtained in earlier trials. In a number of instances, we have terminated the development of product candidates due to a lack of or only modest effectiveness, and clinical trials evaluating our product candidates failed to meet the relevant endpoints. Moreover, even if we obtain positive results from preclinical testing or clinical trials, we may not achieve the same success in future trials, or the FDA and analogous foreign regulatory authorities may deem the results insufficient for an approval.

Many of our clinical trials are conducted under the oversight of IDMCs. These independent oversight bodies are made up of external experts who review the progress of ongoing clinical trials, including available safety and efficacy data, and make recommendations concerning a trial's continuation, modification, or termination based on interim, unblinded data. Any of our ongoing clinical trials may be discontinued or amended in response to recommendations made by responsible IDMCs based on their review of such interim trial results. For example, in August 2020, we discontinued actively treating patients with fasinumab (which at such time only involved dosing in an optional second-year extension phase of one trial) following a recommendation from the responsible IDMC that the program be terminated based on available evidence to date. The recommended termination or material modification of any of our ongoing late-stage clinical trials by an IDMC could negatively impact the future development of our product candidate(s), and our business, prospects, operating results, and financial condition may be materially harmed.

We are studying our product candidates in a wide variety of indications in clinical trials. Many of these trials are exploratory studies designed to evaluate the safety profile of these compounds and to identify what diseases and uses, if any, are best suited for these product candidates. These product candidates may not demonstrate the requisite efficacy and/or safety profile to support continued development for some or all of the indications that are being, or are planned to be, studied, which would diminish our clinical "pipeline" and could negatively affect our future prospects and the value of our Company.

Serious complications or side effects in connection with the use of our products and in clinical trials for our product candidates and new indications for our marketed products could cause our regulatory approvals to be revoked or limited or lead to delay or discontinuation of development of our product candidates or new indications for our marketed products, which could severely harm our business, prospects, operating results, and financial condition.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the drug candidate being studied caused these conditions. Various illnesses, injuries, and discomforts have been reported from time-to-time during clinical trials of our product candidates and new indications for our marketed products. It is possible that as we test our drug candidates or new indications in larger, longer, and more extensive clinical programs, or as use of these drugs becomes more widespread if they receive regulatory approval, illnesses, injuries, and discomforts that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational drugs are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients after approval. If additional clinical experience indicates that any of our product candidates or new indications for our marketed products has many side effects or causes serious or life-threatening side effects, the development of the product candidate may be delayed or fail, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results, and financial condition.

With respect to EYLEA and aflibercept 8 mg, there are many potential safety concerns associated with significant blockade of VEGF that may limit our ability to further successfully commercialize EYLEA and to obtain regulatory approval for aflibercept 8 mg. These serious and potentially life-threatening risks, based on clinical and preclinical experience of VEGF inhibitors, include bleeding, intestinal perforation, hypertension, proteinuria, congestive heart failure, heart attack, and stroke. Other VEGF blockers have reported side effects that became evident only after large-scale trials or after marketing approval when large numbers of patients were treated. There are risks inherent in the intravitreal administration of drugs like aflibercept (such as intraocular inflammation ("IOI"), sterile and culture positive endophthalmitis, corneal decomposition, retinal detachment, and retinal tear), which can cause injury to the eye and other complications. The side effects previously reported for aflibercept include conjunctival hemorrhage, macular degeneration, eye pain, retinal hemorrhage, and vitreous floaters. There is no guarantee that we

will be able to successfully obtain regulatory approval for aflibercept 8 mg. In addition, commercialization of EYLEA or our other products and potential future commercialization of aflibercept 8 mg or our other product candidates may be impacted by actions of third parties on which we rely, such as manufacturers of syringes or other devices used in the administration of our products. These and other complications or issues or side effects could harm further development and/or commercialization of EYLEA as well as further development and potential future commercialization of aflibercept 8 mg.

Dupixent and Libtayo are being studied in additional indications, as shown in the table under Part I, Item 1. "Business - Programs in Clinical Development." There is no guarantee that regulatory approval of Dupixent or Libtayo (as applicable) in any of these indications will be successfully obtained. The side effects previously reported for Dupixent include hypersensitivity reactions, conjunctivitis and keratitis, injection-site reactions, eye and eyelid inflammation, cold sores, oropharyngeal pain, eosinophilia, insomnia, toothache, gastritis, joint pain (arthralgia), and facial rash or redness; and the side effects previously reported for Libtayo include certain immune-mediated adverse reactions, such as pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, and dermatologic reactions, as well as infusion-related reactions, cellulitis, sepsis, pneumonia, urinary tract infection, fatigue, rash, and diarrhea. These and other complications or side effects could harm further development and/or commercialization of Dupixent and Libtayo (as applicable).

There also are risks inherent in subcutaneous injections (which are used for administering most of our antibody-based products and product candidates), such as injection-site reactions (including redness, itching, swelling, pain, and tenderness) and other side effects. These and other complications or side effects could harm further development and/or commercialization of our antibody-based products and product candidates utilizing this method of administration.

Many of our product candidates in development are recombinant proteins that could cause an immune response, resulting in the creation of harmful or neutralizing antibodies against the therapeutic protein.

In addition to the safety, efficacy, manufacturing, and regulatory hurdles faced by our product candidates, the administration of recombinant proteins frequently causes an immune response, resulting in the creation of antibodies against the therapeutic protein. The antibodies can have no effect or can totally neutralize the effectiveness of the protein, or require that higher doses be used to obtain a therapeutic effect. In some cases, the antibody can cross-react with the patient's own proteins, resulting in an "auto-immune" type disease. Whether antibodies will be created can often not be predicted from preclinical or clinical experiments, and their detection or appearance is often delayed, so neutralizing antibodies may be detected at a later date, in some cases even after pivotal clinical trials have been completed.

We may be unable to formulate or manufacture our product candidates in a way that is suitable for clinical or commercial use, which would delay or prevent continued development of such candidates and/or receipt of regulatory approval or commercial sale, which could materially harm our business, prospects, operating results, and financial condition.

If we are unable to continue to develop suitable product formulations or manufacturing processes to support large-scale clinical testing of our product candidates, including our antibody-based product candidates, we may be unable to supply necessary materials for our clinical trials, which would delay or prevent the development of our product candidates. Similarly, if we are unable, directly or through our collaborators or third parties, to supply sufficient quantities of our products or develop formulations of our product candidates suitable for commercial use, we will be unable to obtain regulatory approval for those product candidates.

Many of our products are intended to be used and, if approved, our product candidates may be used in combination with drug-delivery devices, which may result in additional regulatory, commercialization, and other risks.

Many of our products are used and some of our products and product candidates may be used, if approved, in combination with a drug-delivery device, including a pre-filled syringe, patch pump, auto-injector, or other delivery system. For example, in the United States and the EU, EYLEA is approved in the 2mg pre-filled syringe. The success of our products and product candidates may depend to a significant extent on the performance of such devices, some of which may be novel or comprised of complex components. Given the increased complexity of the review process when approval of the product and device is sought under a single marketing application and the additional risks resulting from a product candidate's designation as a combination product discussed below, our product candidates used with such drug-delivery devices may be substantially delayed in receiving regulatory approval or may not be approved at all. The FDA review process and criteria for such applications are not well established, which could also lead to delays in the approval process. In addition, some of these drug-delivery devices may be provided by single-source, third-party providers or our collaborators. In any such case, we may be dependent on the sustained cooperation of those third-party providers or collaborators to supply and manufacture the devices; to conduct the studies and prepare related documentation required for approval or clearance by the applicable regulatory agencies; and to continue to meet the applicable regulatory and other requirements to maintain approval or clearance once it has been received. In addition, other parties may allege that our drug-delivery devices infringe patents or other intellectual property rights. For example, we are currently party to patent infringement and other proceedings relating to the EYLEA pre-filled syringe, as described in Note 15 to

our Consolidated Financial Statements. Failure to successfully develop or supply the devices, delays in or failure of the studies conducted by us, our collaborators, or third-party providers, or failure of our Company, our collaborators, or the third-party providers to obtain or maintain regulatory approval or clearance of the devices could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in a product or product candidate reaching the market. Loss of regulatory approval or clearance of a device that is used with our product may also result in the removal of our product from the market. Further, failure to successfully develop or supply and manufacture these devices, or to gain or maintain their approval, could adversely affect sales of the related products.

In the United States, each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a drug, biologic, or device. The determination whether a product is a combination product or two separately regulated products is made by the FDA on a case-by-case basis. Although a single marketing application is generally sufficient for the approval, clearance, or licensure of a combination product, the FDA may determine that separate marketing applications are necessary. In addition, submitting separate marketing applications may be necessary to receive some benefit that accrues only from approval under a particular type of application. This could significantly increase the resources and time required to bring a particular combination product to market.

Risks Related to Intellectual Property and Market Exclusivity

For purposes of this subsection, references to our intellectual property (including patents, trademarks, copyrights, and trade secrets) include that of our collaborators and licensees, unless otherwise stated or required by the context.

If we cannot protect the confidentiality of our trade secrets, or our patents or other means of defending our intellectual property are insufficient to protect our proprietary rights, our business and competitive position will be harmed.

Our business requires using sensitive and proprietary technology and other information that we protect as trade secrets. We seek to prevent improper disclosure of these trade secrets through confidentiality agreements and other means. If our trade secrets are improperly disclosed, by our current or former employees, our collaborators, or otherwise, it could help our competitors and adversely affect our business. We will be able to protect our proprietary rights only to the extent that our proprietary technologies and other information are covered by valid and enforceable patents or are effectively maintained as trade secrets. The patent position of biotechnology companies, including our Company, involves complex legal and factual questions and, therefore, enforceability cannot be predicted with certainty. Our patents may be challenged, invalidated, held to be unenforceable, or circumvented. For example, certain of our U.S. patents (including those pertaining to our key products, such as EYLEA) have been and may in the future be challenged by parties who file a request for post-grant review or *inter partes* review under the America Invents Act of 2011 or *ex parte* reexamination, as described in Note 15 to our Consolidated Financial Statements included in this report. Post-grant proceedings are increasingly common in the United States and are costly to defend. In addition, patent applications filed outside the United States may be challenged by other parties, for example, by filing third-party observations that argue against patentability or an opposition. Such opposition proceedings are increasingly common in the EU and are costly to defend. For example, our European Patent No. 2,264,163 (which concerns genetically engineered mice capable of producing chimeric antibodies that are part human and part mouse) is the subject of opposition proceedings in the European Patent Office (the "EPO") (currently pending before its Boards of Appeal). In addition, on October 26 and October 27, 2021, anonymous parties initiated opposition proceedings in the EPO against our European Patent No. 2,944,306 (which concerns pre-filled syringes comprising ophthalmic formulations containing VEGF antagonists such as aflibercept for intravitreal administration), as described in Note 15 to our Consolidated Financial Statements included in this report. We have pending patent applications in the United States Patent and Trademark Office (the "USPTO"), the EPO, and the patent offices of other foreign jurisdictions, and it is likely that we will need to defend patents from challenges by others from time to time in the future. Our patent rights may not provide us with a proprietary position or competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be extremely expensive and time consuming.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions or our ability to obtain, maintain, and enforce our intellectual property rights. Any such changes could also affect the value of our intellectual property or narrow the scope of our patents. For example, the World Trade Organization ("WTO") is currently considering a proposal formulated in connection with the COVID-19 pandemic for a waiver of certain intellectual property rights under the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights; the ultimate timing and scope of this waiver is unknown and we cannot be certain that our intellectual property rights related to REGEN-COV or any other current or future product or product candidate or technology would not be eliminated, narrowed, or weakened by any such waiver.

We also currently hold issued trademark registrations and have trademark applications pending in the United States and other jurisdictions, any of which may be the subject of a governmental or third-party objection, which could prevent the maintenance or issuance of the trademark. As our products mature, our reliance on our trademarks to differentiate us from our competitors increases and as a result, if we are unable to prevent third parties from adopting, registering, or using trademarks that infringe, dilute or otherwise violate our trademark rights, our business could be adversely affected.

We may be restricted in our development, manufacturing, and/or commercialization activities by patents or other proprietary rights of others, and could be subject to awards of damages if we are found to have infringed such patents or rights.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of others (including those relating to trademarks, copyrights, and trade secrets). Other parties may allege that they own blocking patents to our products in clinical development or even to products that have received regulatory approval and are being or have been commercialized, either because they claim to hold proprietary rights to the composition of a product or the way it is manufactured or the way it is used. Moreover, other parties may allege that they have blocking patents to antibody-based products made using our *VelocImmune* technology, or any other of our technologies, either because of the way the antibodies are discovered or produced or because of a proprietary composition covering an antibody or the antibody's target.

We have been in the past, are currently, and may in the future be involved in patent litigation and other proceedings involving patents and other intellectual property. For example, we and/or Sanofi are currently party to patent infringement proceedings initiated by Amgen against us and/or Sanofi relating to Praluent and other intellectual property proceedings relating to Dupixent, as described in Note 15 to our Consolidated Financial Statements. In addition, we are currently party to patent infringement and other proceedings relating to EYLEA and REGEN-COV, as described in Note 15 to our Consolidated Financial Statements.

We are aware of patents and pending patent applications owned by others that claim compositions and methods of treatment relating to targets and conditions that we are also pursuing with our products and/or product candidates. Although we do not believe that any of our products or our late-stage antibody-based product candidates infringe any valid claim in these patents or patent applications, these other parties could initiate lawsuits for patent infringement and assert that their patents are valid and cover our products or our late-stage antibody-based product candidates, similar to the patent infringement proceedings referred to above. Further, we are aware of a number of patent applications of others that, if granted with claims as currently drafted, may cover our current or planned activities. It could be determined that our products and/or actions in manufacturing or selling our products or product candidates infringe such patents.

Patent holders could assert claims against us for damages and seek to prevent us from manufacturing, selling, or developing our products or product candidates, and a court may find that we are infringing validly issued patents of others. In the event that the manufacture, use, or sale of any of our products or product candidates infringes on the patents or violates other proprietary rights of others, we may be prevented from pursuing product development, manufacturing, and commercialization of those drugs and may be required to pay costly damages. In addition, in the event that we assert our patent rights against other parties that we believe are infringing our patent rights, such parties may challenge the validity of our patents and we may become the target of litigation, which may result in an outcome that is unfavorable to us. Any of these adverse developments may materially harm our business, prospects, operating results, and financial condition. In any event, legal disputes are likely to be costly and time consuming to defend.

We seek to obtain licenses to patents when, in our judgment, such licenses are needed or advisable. For example, in August 2018, we and Sanofi entered into a license agreement with Bristol-Myers Squibb, E. R. Squibb & Sons, and Ono Pharmaceutical to obtain a license under certain patents owned and/or exclusively licensed by one or more of these parties that includes the right to develop and sell Libtayo. If any licenses are required, we may not be able to obtain such licenses on commercially reasonable terms, if at all. The failure to obtain any such license could prevent us from developing or commercializing any one or more of our products or product candidates, which could severely harm our business.

In addition, other parties may have regulatory exclusivity in the United States or foreign jurisdictions for products relating to targets or conditions we are also pursuing, which could prevent or delay our ability to apply for or obtain regulatory approval for our product candidates in such jurisdictions. For example, in the EU, a designated orphan drug is provided up to 10 years of market exclusivity in the orphan indication, during which time the EMA is generally precluded from accepting a MAA for a similar medicinal product unless it can be demonstrated that it is safer, more effective, or otherwise clinically superior to the original orphan medicinal product.

Loss or limitation of patent rights, and regulatory pathways for biosimilar competition, could reduce the duration of market exclusivity for our products.

In the pharmaceutical and biotechnology industries, the majority of an innovative product's commercial value is usually realized during the period in which it has market exclusivity. In the United States and some other countries, when market exclusivity expires and generic versions of a product are approved and marketed, there usually are very substantial and rapid declines in the product's sales.

If our late-stage product candidates or other clinical candidates are approved for marketing in the United States or elsewhere, market exclusivity for those products will generally be based upon patent rights and/or certain regulatory forms of exclusivity. As described above under "*If we cannot protect the confidentiality of our trade secrets, or our patents or other means of defending our intellectual property are insufficient to protect our proprietary rights, our business and competitive position will be harmed,*" the scope and enforceability of our patent rights may vary from country to country. The failure to obtain patent and other intellectual property rights, or limitations on the use, or the loss, of such rights could materially harm us. Absent patent protection or regulatory exclusivity for our products, it is possible, both in the United States and elsewhere, that generic, biosimilar, and/or interchangeable versions of those products may be approved and marketed, which would likely result in substantial and rapid reductions in revenues from sales of those products.

Under the PPACA, there is an abbreviated path in the United States for regulatory approval of products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-approved biological product. The PPACA provides a regulatory mechanism that allows for FDA approval of biologic drugs that are similar to innovative drugs on the basis of less extensive data than is required by a full BLA. Under this regulation, an application for approval of a biosimilar may be filed four years after approval of the innovator product. However, qualified innovative biological products receive 12 years of regulatory exclusivity, meaning that the FDA may not approve a biosimilar version until 12 years after the innovative biological product was first approved by the FDA. However, the term of regulatory exclusivity may not remain at 12 years in the United States and could be shortened if, for example, the PPACA is amended.

A number of jurisdictions outside of the United States have also established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier versions of biological products. For example, the EU has had an established regulatory pathway for biosimilars since 2005.

The increased likelihood of biosimilar competition has increased the risk of loss of innovators' market exclusivity. It is also not possible to predict changes in United States regulatory law that might reduce biological product regulatory exclusivity. Due to this risk, and uncertainties regarding patent protection, it is not possible to predict the length of market exclusivity for any particular product we currently or may in the future commercialize with certainty based solely on the expiration of the relevant patent(s) or the current forms of regulatory exclusivity. We are aware of several companies developing biosimilar versions of EYLEA, as discussed further under "Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *The commercial success of our products and product candidates is subject to significant competition* - Marketed Products" above. In the United States, the regulatory exclusivity period for EYLEA (i.e., the period during which no biosimilar product can be approved by the FDA) expires on November 18, 2023, with the possibility of an additional six months of regulatory exclusivity (i.e., until May 18, 2024) if the FDA grants pediatric exclusivity based on our completion of certain studies evaluating EYLEA in pediatric patients with ROP and submission of the data from these studies to the FDA no later than 15 months before the date on which regulatory exclusivity would otherwise expire. The loss of market exclusivity for a product (such as EYLEA) would likely materially and negatively affect revenues from product sales of that product and thus our financial results and condition.

Risks Related to Manufacturing and Supply

We rely on limited internal and contracted manufacturing and supply chain capacity, which could adversely affect our ability to commercialize our marketed products and, if approved, our product candidates and to advance our clinical pipeline.

We have large-scale manufacturing operations in Rensselaer, New York and Limerick, Ireland. Manufacturing facilities operated by us and by third-party contract manufacturers engaged by us would be inadequate to produce the active pharmaceutical ingredients of our current marketed products and our product candidates in sufficient clinical quantities if our clinical pipeline advances as planned. For example, our internal and contracted manufacturing capacity may not be sufficient to cover the demand for REGEN-COV and our other COVID-19 monoclonal antibodies (if successfully developed and authorized for use). In addition to expanding our internal capacity, we intend to continue to rely on our collaborators, and may also rely on contract manufacturers, to produce commercial quantities of drug material needed for commercialization of our products. For example, as described in Part I, Item 1. "Business," in August 2020, we announced a collaboration agreement with Roche to develop, manufacture, and distribute REGEN-COV (known as Ronapreve in other countries outside the United States). We cannot be certain that our current manufacturing and distribution capacity for REGEN-COV or the increased manufacturing and distribution

capacity through our collaboration with Roche will be sufficient if there is significant future demand for REGEN-COV. As we increase our production in anticipation of potential regulatory approval for our product candidates, our current manufacturing capacity will likely not be sufficient, and our dependence on our collaborators and/or contract manufacturers may increase, to produce adequate quantities of drug material for both commercial and clinical purposes. We also rely entirely on other parties and our collaborators for filling and finishing services. Generally, in order for other parties to perform any step in the manufacturing and supply chain, we must transfer technology to the other party, which can be time consuming and may not be successfully accomplished without considerable cost and expense, or at all. We will have to depend on these other parties to perform effectively on a timely basis and to comply with regulatory requirements. If for any reason they are unable to do so, and as a result we are unable to directly or through other parties manufacture and supply sufficient commercial and clinical quantities of our products on acceptable terms, or if we should encounter delays or other difficulties with our collaborators, contract manufacturers, warehouses, shipping, testing laboratories, or other parties involved in our supply chain which adversely affect the timely manufacture and supply of our products or product candidates, our business, prospects, operating results, and financial condition may be materially harmed.

Expanding our manufacturing capacity and establishing fill/finish capabilities will be costly and we may be unsuccessful in doing so in a timely manner, which could delay or prevent the launch and successful commercialization of our marketed products and product candidates or other indications for our marketed products if they are approved for marketing and could jeopardize our current and future clinical development programs.

In addition to our existing manufacturing facilities in Rensselaer, New York and Limerick, Ireland, we may lease, operate, purchase, or construct additional facilities to conduct expanded manufacturing or other related activities in the future. Expanding our manufacturing capacity to supply commercial quantities of the active pharmaceutical ingredients for our marketed products and our product candidates if they are approved for marketing, and to supply clinical drug material to support the continued growth of our clinical programs, will require substantial additional expenditures, time, and various regulatory approvals and permits. This also holds true for establishing fill/finish capabilities in the future, for which we are in the process of constructing fill/finish facilities (refer to Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations – Liquidity and Capital Resources" for information about expected capital expenditures relating to this and other projects). Further, we will need to hire and train significant numbers of employees and managerial personnel to staff our expanding manufacturing and supply chain operations, as well as any future fill/finish activities. Start-up costs can be large, and scale-up entails significant risks related to process development and manufacturing yields. In addition, we may face difficulties or delays in developing or acquiring the necessary production equipment and technology to manufacture sufficient quantities of our product candidates at reasonable costs and in compliance with applicable regulatory requirements. The FDA and analogous foreign regulatory authorities must determine that our existing and any expanded manufacturing facilities and any future fill/finish activities comply, or continue to comply, with cGMP requirements for both clinical and commercial production and license them, or continue to license them, accordingly, and such facilities must also comply with applicable environmental, safety, and other governmental permitting requirements. We may not successfully expand or establish sufficient manufacturing or any future fill/finish capabilities or manufacture our products economically or in compliance with cGMPs and other regulatory requirements, and we and our collaborators may not be able to build or procure additional capacity in the required timeframe to meet commercial demand for our product candidates if they receive regulatory approval, and to continue to meet the requirements of our clinical programs. This would interfere with our efforts to successfully commercialize our marketed products, and could also delay or require us to discontinue one or more of our clinical development programs. As a result, our business, prospects, operating results, and financial condition could be materially harmed.

Our ability to manufacture products may be impaired if any of our or our collaborators' manufacturing activities, or the activities of other third parties involved in our manufacture and supply chain, are found to infringe patents of others.

Our ability to continue to manufacture products in our Rensselaer, New York and Limerick, Ireland facilities and at additional facilities (if any) in the future (including our ability to conduct any fill/finish activities in the future), the ability of our collaborators to manufacture products at their facilities, and our ability to utilize other third parties to produce our products, to supply raw materials or other products, or to perform fill/finish services or other steps in our manufacture and supply chain, depends on our and their ability to operate without infringing the patents or other intellectual property rights of others. Other parties may allege that our or our collaborators' manufacturing activities, or the activities of other third parties involved in our manufacture and supply chain (which may be located in jurisdictions outside the United States), infringe patents or other intellectual property rights. For example, we are currently party to patent infringement and other proceedings relating to the EYLEA pre-filled syringe, as described in Note 15 to our Consolidated Financial Statements. A judicial or regulatory decision in favor of one or more parties making such allegations could directly or indirectly preclude the manufacture of our products to which those intellectual property rights apply on a temporary or permanent basis, which could materially harm our business, prospects, operating results, and financial condition.

If sales of our marketed products do not meet the levels currently expected, or if the launch of any of our product candidates is delayed or unsuccessful, we may face costs related to excess inventory or unused capacity at our manufacturing facilities and at the facilities of third parties or our collaborators.

We use our manufacturing facilities primarily to produce bulk product for commercial supply of our marketed products and clinical and preclinical candidates for ourselves and our collaborations. We also plan to use such facilities to produce bulk product for commercial supply of new indications of our marketed products and new product candidates if they are approved for marketing or otherwise authorized for use. If our clinical candidates are discontinued or their clinical development is delayed, if the launch of new indications for our marketed products or new product candidates is delayed or does not occur, or if such products are launched and the launch is unsuccessful or the product is subsequently recalled or marketing approval is rescinded, we may have to absorb one hundred percent of related overhead costs and inefficiencies, as well as similar costs of third-party contract manufacturers performing services for us. In addition, if we or our collaborators experience excess inventory, it may be necessary to write down or write off such excess inventory or incur an impairment charge with respect to the facility where such product is manufactured, which could adversely affect our operating results. For example, during the fourth quarter of 2021, we recorded a charge of $231.7 million to write down REGEN-COV inventory, as described in Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Results of Operations."

Third-party service or supply failures, or other failures, business interruptions, or other disasters affecting our manufacturing facilities in Rensselaer, New York and Limerick, Ireland, the manufacturing facilities of our collaborators, or the facilities of any other party participating in the supply chain, would adversely affect our ability to supply our products.

Bulk drug materials are currently manufactured at our manufacturing facilities in Rensselaer, New York and Limerick, Ireland, as well as at our collaborators' facilities. We and our collaborators would be unable to manufacture these materials if the relevant facility were to cease production due to regulatory requirements or actions, business interruptions, labor shortages or disputes, contaminations, fire, climate change, natural disasters, acts of war or terrorism, or other problems.

Many of our products and product candidates are very difficult to manufacture. As our products and most of our product candidates are biologics, they require processing steps that are more difficult than those required for many other chemical pharmaceuticals. Accordingly, multiple steps are needed to control the manufacturing processes. Problems with these manufacturing processes, even minor deviations from the normal process or from the materials used in the manufacturing process (which may not be detectable by us or our collaborators in a timely manner), could lead to product defects or manufacturing failures, resulting in lot failures, product recalls, product liability claims, and insufficient inventory. Also, the complexity of our manufacturing process may make it difficult, time-consuming, and expensive to transfer our technology to our collaborators or contract manufacturers.

Also, certain raw materials or other products necessary for the manufacture and formulation of our marketed products and product candidates, some of which are difficult to source, are provided by single-source unaffiliated third-party suppliers. In addition, we rely on certain third parties or our collaborators to perform filling, finishing, distribution, laboratory testing, and other services related to the manufacture of our marketed products and product candidates, and to supply various raw materials and other products. We would be unable to obtain these raw materials, other products, or services for an indeterminate period of time if any of these third parties were to cease or interrupt production or otherwise fail to supply these materials, products, or services to us for any reason, including due to regulatory requirements or actions (including recalls), adverse financial developments at or affecting the supplier, failure by the supplier to comply with cGMPs, contaminations, business interruptions, or labor shortages or disputes (in each case, including as a result of the COVID-19 pandemic, which has exacerbated many of these issues). In any such circumstances, we may not be able to engage a backup or alternative supplier or service provider in a timely manner or at all. This, in turn, could materially and adversely affect our or our collaborators' ability to manufacture or supply marketed products and product candidates, which could materially and adversely affect our business and future prospects.

Certain of the raw materials required in the manufacture and testing of our products and product candidates may be derived from biological sources, including mammalian tissues, bovine serum, and human serum albumin. There are certain regulatory restrictions on using these biological source materials. If we or our collaborators are required to substitute for these sources to comply with such regulatory requirements, our clinical development or commercial activities may be delayed or interrupted.

Our or our collaborators' failure to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates could result in incurring substantial remedial costs, delays in the development or approval of our product candidates or new indications for our marketed products and/or in their commercial launch if regulatory approval is obtained, and a reduction in sales.

We and our collaborators and other third-party providers are required to maintain compliance with cGMPs, and are subject to inspections by the FDA or comparable agencies in other jurisdictions to confirm such compliance. Changes of suppliers or modifications of methods of manufacturing may require amending our application(s) to the FDA or such comparable foreign agencies and acceptance of the change by the FDA or such comparable foreign agencies prior to release of product(s). Because we produce multiple products and product candidates at our facilities in Rensselaer, New York and Limerick, Ireland, there are increased risks associated with cGMP compliance. Our inability, or the inability of our collaborators and third-party fill/finish or other service providers, to demonstrate ongoing cGMP compliance could require us to engage in lengthy and expensive remediation efforts, withdraw or recall product, halt or interrupt clinical trials, and/or interrupt commercial supply of any marketed products, and could also delay or prevent our obtaining regulatory approval for our product candidates or new indications for our marketed products. Any delay, interruption, or other issue that arises in the manufacture, fill/finish, packaging, or storage of any drug product or product candidate as a result of a failure of our facilities or the facilities or operations of our collaborators or other third parties to pass any regulatory agency inspection or maintain cGMP compliance could significantly impair our ability to develop, obtain approval for, and successfully commercialize our products, which would substantially harm our business, prospects, operating results, and financial condition. Any finding of non-compliance could also increase our costs, cause us to delay the development of our product candidates, result in delay in our obtaining, or our not obtaining, regulatory approval of product candidates or new indications for our marketed products, and cause us to lose revenue from any marketed products, which could be seriously detrimental to our business, prospects, operating results, and financial condition. Significant noncompliance could also result in the imposition of monetary penalties or other civil or criminal sanctions and damage our reputation.

Other Regulatory and Litigation Risks

If the testing or use of our products harms people, or is perceived to harm them even when such harm is unrelated to our products, we could be subject to costly and damaging product liability claims.

The testing, manufacturing, marketing, and sale of drugs for use in people expose us to product liability risk. Any informed consent or waivers obtained from people who enroll in our clinical trials may not protect us from liability or the cost of litigation. We may also be subject to claims by patients who use our approved products, or our product candidates if those product candidates receive regulatory approval and become commercially available, that they have been injured by a side effect associated with the drug. Even in a circumstance in which we do not believe that an adverse event is related to our products or product candidates, the related investigation may be time consuming or inconclusive and may have a negative impact on our reputation or business. We may face product liability claims and be found responsible even if injury arises from the acts or omissions of third parties who provide fill/finish or other services. To the extent we maintain product liability insurance in relevant periods, such insurance may not cover all potential liabilities or may not completely cover any liability arising from any such litigation. Moreover, in the future we may not have access to liability insurance or be able to maintain our insurance on acceptable terms.

Our business activities have been, and may in the future be, challenged under federal or state healthcare laws, which may subject us to civil or criminal proceedings, investigations, or penalties.

The FDA regulates the marketing and promotion of our products, which must comply with the Food, Drug, and Cosmetic Act and applicable FDA implementing standards. The FDA's review of promotional activities includes healthcare provider-directed and direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and sales representatives' communications. Failure to comply with applicable FDA requirements and restrictions in this area may subject a company to adverse publicity and enforcement action by the FDA, the Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes a drug. The FDA may take enforcement action for promoting unapproved uses of a product or other violations of its advertising laws and regulations. The applicable regulations in countries outside the U.S. grant similar powers to the competent authorities and impose similar obligations on companies.

In addition to FDA and related regulatory requirements, we are subject to health care "fraud and abuse" laws, such as the federal civil False Claims Act, the anti-kickback provisions of the federal Social Security Act, and other state and federal laws and regulations. The U.S. federal healthcare program anti-kickback statute (the "AKS") prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving payments or other remuneration, directly or indirectly, to induce or reward someone to purchase, prescribe, endorse, arrange for, or recommend a product or service that is reimbursed under federal healthcare programs such as Medicare or Medicaid. If we provide payments or other remuneration to a healthcare professional to induce the prescribing of our products, we could face liability under state and federal anti-kickback laws. Recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the federal anti-kickback statute.

The federal civil False Claims Act prohibits any person from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. Pharmaceutical companies have been investigated and/or prosecuted under these laws for a variety of alleged promotional and marketing activities, such as allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in promotion for uses that the FDA has not approved, known as off-label uses, that caused claims to be submitted to Medicaid for non-covered off-label uses; and submitting inflated best price information to the Medicaid Rebate program. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal fraud and false statement statutes that extend to non-government health benefit programs.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, damages, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment for individuals and the curtailment or restructuring of operations. Even if it is determined that we have not violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which would harm our business, prospects, operating results, and financial condition. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be challenged under one or more of such laws. As described further in Note 15 to our Consolidated Financial Statements included in this report, we are party to a civil complaint filed in June 2020 by the U.S. Attorney's Office for the District of Massachusetts concerning our support of a 501(c)(3) organization that provides financial assistance to patients; and we are cooperating with pending government investigations concerning certain other business activities. Any adverse decision, finding, allegation, or exercise of enforcement or regulatory discretion in any such proceedings or investigations could harm our business, prospects, operating results, and financial condition.

As part of the PPACA, the federal government requires that pharmaceutical manufacturers record any "transfers of value" made to U.S. licensed physicians and teaching hospitals as well as ownership and investment interests held by physicians and their immediate family members. Information provided by companies is aggregated and posted annually on an "Open Payments" website, which is managed by CMS, the agency responsible for implementing these disclosure requirements. Beginning in 2022, applicable manufacturers also will be required to report information (starting with information collected during 2021) regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants, and certified nurse-midwives.

We continue to dedicate significant resources to comply with these requirements and need to be prepared to comply with additional reporting obligations outside the United States that may apply in the future. In addition, several states have legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities; restrict when pharmaceutical companies may provide meals or gifts to prescribers or engage in other marketing-related activities; require identification or licensing of sales representatives; and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Many of these requirements and standards are new or uncertain, and the penalties for failure to comply with these requirements may be unclear. If we are found not to be in full compliance with these laws, we could face enforcement actions, fines, and other penalties, and could receive adverse publicity, which would harm our business, prospects, operating results, and financial condition. Additionally, access to such data by fraud-and-abuse investigators and industry critics may draw scrutiny to our collaborations with reported entities.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations, and future prospects.

We participate in the Medicaid Drug Rebate program, the Public Health Service's 340B drug pricing program (the "340B program"), the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program, and the Tricare Retail Pharmacy Program. See Part I, Item 1, "Business - Government Regulation - Pricing and Reimbursement" for a description of these programs.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. Such interpretation can change and evolve over time. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. CMS could also decide to terminate our Medicaid drug rebate agreement, or HRSA could decide to terminate our 340B program participation agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs.

Our failure to comply with our reporting and payment obligations under the Medicaid Drug Rebate program and other governmental programs could negatively impact our financial results. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the PPACA. The final regulation has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we have taken in our implementation of the final regulation. Other regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program may have a similar impact.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. Implementation of this regulation has affected our obligations and potential liability under the 340B program. We are also required to report the 340B ceiling prices for our covered outpatient drugs to HRSA, which then publishes them to 340B covered entities. Any charge by HRSA that we have violated the requirements of the program or the regulation could negatively impact our financial results. Moreover, under a final regulation effective January 13, 2021, HRSA newly established an ADR process for claims by covered entities that a manufacturer has engaged in overcharging, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. An ADR proceeding could subject us to onerous procedural requirements and could result in additional liability. Further, any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the PPACA or otherwise could affect our 340B ceiling price calculations and negatively impact our results of operations.

We have obligations to report the average sales price for certain of our drugs to the Medicare program as a part of our agreement to participate in the Medicaid Drug Rebate program. For calendar quarters beginning January 1, 2022, we will need to report the average sales price for certain drugs under the Medicare program regardless of whether we participate in the Medicaid Drug Rebate program. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations.

Starting in 2023, manufacturers must pay refunds to Medicare for single-source drugs or biological products, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125 percent of the refund amount.

Pursuant to applicable law, knowing provision of false information in connection with price reporting or contract-based requirements under the VA/FSS and/or Tricare programs can subject a manufacturer to civil monetary penalties. These program and contract-based obligations also contain extensive disclosure and certification requirements. If we overcharge the government in connection with our arrangements with FSS or Tricare, we are required to refund the difference to the government. Failure to make necessary disclosures or to identify contract overcharges can result in allegations against us under the False Claims Act and

other laws and regulations. Unexpected refunds to the government, and/or response to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations, and future prospects.

Risks from the improper conduct of employees, agents, contractors, or collaborators could adversely affect our reputation and our business, prospects, operating results, and financial condition.

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors, or collaborators that would violate the laws or regulations of the jurisdictions in which we operate, including, without limitation, healthcare, employment, foreign corrupt practices, trade restrictions and sanctions, environmental, competition, and privacy laws and regulations. Such improper actions could subject us to civil or criminal investigations, and monetary and injunctive penalties, and could adversely impact our ability to conduct business, operating results, and reputation.

In particular, our business activities outside the United States are subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our ability to expand internationally, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Our operations are subject to environmental, health, and safety laws and regulations, including those governing the use of hazardous materials. Compliance with these laws and regulations is costly, and we may incur substantial liability arising from our activities involving the use of hazardous materials.

As a fully integrated biotechnology company with significant research and development and manufacturing operations, we are subject to extensive environmental, health, and safety laws and regulations, including those governing the use of hazardous materials. Our research and development and manufacturing activities involve the controlled use of chemicals, infectious agents (such as viruses, bacteria, and fungi), radioactive compounds, and other hazardous materials. The cost of compliance with environmental, health, and safety regulations is substantial. If an accident involving these materials or an environmental discharge were to occur, we could be held liable for any resulting damages, or face regulatory actions, which could exceed our resources or insurance coverage.

Our business is subject to increasingly complex corporate governance, public disclosure, and accounting requirements and regulations that could adversely affect our business, operating results, and financial condition.

We are subject to changing rules and regulations of various federal and state governmental authorities as well as the stock exchange on which our Common Stock is listed. These entities, including the SEC and The NASDAQ Stock Market LLC, have issued a significant number of new and increasingly complex requirements and regulations over the course of the last several years and continue to develop additional requirements and regulations. For example, there are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Wall Street Reform and Protection Act that expressly authorized or required the SEC to adopt additional rules in these areas, a number of which have yet to be fully implemented. Our efforts to comply with these requirements and regulations (as well as corporate governance and disclosure expectations of investors and other stakeholders) have resulted in, and are likely to continue to result in, an increase in expenses and a diversion of management's time from other business activities.

Changes in laws and regulations affecting the healthcare industry could adversely affect our business.

All aspects of our business, including research and development, manufacturing, marketing, pricing, sales, intellectual property rights, and the framework for dispute resolution and asserting our rights against others, are subject to extensive legislation and regulation. Changes in applicable federal and state laws and agency regulations could have a materially negative impact on our business. These include:

- changes in the FDA and foreign regulatory processes for new therapeutics that may delay or prevent the approval of any of our current or future product candidates;
- new laws, regulations, or judicial decisions related to healthcare availability or the payment for healthcare products and services, including prescription drugs, that would make it more difficult for us to market and sell products once they are approved by the FDA or foreign regulatory agencies;
- changes in FDA and foreign regulations that may require additional safety monitoring prior to or after the introduction of new products to market, which could materially increase our costs of doing business; and
- changes in FDA and foreign cGMP requirements that may make it more difficult and costly for us to maintain regulatory compliance and/or manufacture our marketed product and product candidates in accordance with cGMPs.

As described above, the PPACA and potential regulations thereunder easing the entry of competing follow-on biologics into the marketplace, other new legislation or implementation of existing statutory provisions on importation of lower-cost competing drugs from other jurisdictions, and legislation on comparative effectiveness research are examples of previously enacted and possible future changes in laws that could adversely affect our business.

The U.S. government could carry out other significant changes in legislation, regulation, and government policy, including with respect to government reimbursement changes and drug price control measures (such as those discussed above under "Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *Sales of our marketed products are dependent on the availability and extent of reimbursement from third-party payors, and changes to such reimbursement may materially harm our business, prospects, operating results, and financial condition*"). While it is not possible to predict whether and when any such changes will occur, changes in the laws, regulations, and policies governing the development and approval of our product candidates and the commercialization, importation, and reimbursement of our products could adversely affect our business. In addition, our development and commercialization activities could be harmed or delayed by a shutdown of the U.S. government, including the FDA. For example, a prolonged shutdown may significantly delay the FDA's ability to timely review and process any submissions we have filed or may file or cause other regulatory delays, which could materially and adversely affect our business.

Risks associated with our operations outside the United States could adversely affect our business.

We have operations and conduct business outside the United States and we plan to expand these activities. For example, we recently commenced co-commercialization activities under the Antibody Collaboration related to Dupixent in certain jurisdictions outside the United States. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries, which include:

- unfamiliar foreign laws or regulatory requirements or unexpected changes to those laws or requirements, including those with which we and/or our collaborators must comply in order to maintain our marketing authorizations outside the United States;
- other laws and regulatory requirements to which our business activities abroad are subject, such as the FCPA and the U.K. Bribery Act (discussed in greater detail above under "*Risks from the improper conduct of employees, agents, contractors, or collaborators could adversely affect our reputation and our business, prospects, operating results, and financial condition*");
- changes in the political or economic condition of a specific country or region;
- fluctuations in the value of foreign currency versus the U.S. dollar;
- tariffs, trade protection measures, import or export licensing requirements, trade embargoes, and sanctions (including those administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury), and other trade barriers;
- difficulties in attracting and retaining qualified personnel; and
- cultural differences in the conduct of business.

For example, effective January 31, 2020, the United Kingdom commenced an exit from the EU, commonly referred to as "Brexit." The transition period for Brexit expired on December 31, 2020 following the entry into a trade agreement that now governs the United Kingdom's relationship with the EU. We do not know to what extent Brexit will ultimately impact the business and regulatory environment in the United Kingdom, the rest of the EU, or other countries. For example, the impact of Brexit on the ongoing validity in the United Kingdom of current EU authorizations for medicinal products and on the future

process for obtaining and maintaining marketing authorization for pharmaceutical products manufactured or sold in the United Kingdom remains uncertain. We have large-scale manufacturing operations in Limerick, Ireland and have also established an office in the vicinity of London. Changes impacting our ability to conduct business in the United Kingdom or other EU countries, or changes to the regulatory regime applicable to our operations in those countries (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition.

We may incur additional tax liabilities related to our operations.

We are subject to income tax in the United States and various foreign jurisdictions. Significant judgment is required in determining our worldwide tax liabilities, and our effective tax rate is derived from a combination of the applicable statutory rates in the various jurisdictions in which we operate. We record liabilities for uncertain tax positions that involve significant management judgment as to the application of law. The Internal Revenue Service or other domestic or foreign taxing authorities have previously disagreed, and may in the future disagree, with our interpretation of tax law as applied to the operations of Regeneron and its subsidiaries or with the positions we may take with respect to particular tax issues on our tax returns (see also Note 14 to our Consolidated Financial Statements included in this report). Consequently, our reported effective tax rate and our after-tax cash flows may be materially and adversely affected by tax assessments or judgments in excess of accrued amounts we have estimated in preparing our financial statements. Further, our effective tax rate may also be adversely affected by numerous other factors, including changes in the mix of our profitability from country to country, changes in tax laws and regulations, and tax effects of the accounting for stock-based compensation (which depend in part on the price of our stock and, therefore, are beyond our control). Changes to U.S. tax laws and/or recommendations from the Organization for Economic Co-operation and Development (the "OECD") regarding a global minimum tax and other changes being considered and/or implemented in countries where we operate could materially impact our tax provision, cash tax liability, and effective tax rate. In addition, recommendations by the OECD and the EU could require companies to disclose more information to tax authorities on operations around the world, which may lead to greater audit scrutiny. Even though we regularly assess the information provided to tax authorities in determining the appropriateness of our tax reserves, such tax authorities could take a position that is contrary to our expectations, and the result could adversely affect our provision for income tax and our current rate.

We face risks related to the personal data we collect, process, and share.

Our ability to conduct our business is significantly dependent on the data that we collect, process, and share in discovering and developing drug products. These data are often considered personal data and are therefore regulated by data privacy laws in applicable jurisdictions.

Our clinical trial programs and research collaborations outside the U.S. (such as our consortium with a group of companies to fund the generation of genetic exome sequence data from the UK Biobank health resource) implicate non-U.S. data protection laws, including the GDPR. The GDPR has a range of compliance obligations, including increased transparency requirements and data subject rights. Violations of the GDPR carry significant financial penalties for noncompliance (including possible fines of up to 4% of global annual turnover for the preceding financial year or €20 million (whichever is higher)). In addition to the GDPR, certain EU Member States have issued or will be issuing their own implementation legislation. In June 2021, the European Commission introduced new standard contractual clauses required to be incorporated into new and existing agreements within prescribed timeframes in order to continue to lawfully transfer personal data outside the EU. Compliance with these requirements has been and is expected to continue to be costly and time consuming.

We conduct clinical trials in many countries around the world, which have new or evolving data privacy laws that have resulted in increased liability in the management of clinical trial data, and additional contractual and due-diligence obligations that could lead to a delay in clinical trial site start-up. While we continue to monitor these developments, there remains some uncertainty surrounding the legal and regulatory environment for these evolving privacy and data protection laws. Complying with varying jurisdictional requirements could increase the costs and complexity of compliance, including the risk of substantial financial penalties for insufficient notice and consent, failure to respond to data subject rights requests, lack of a legal basis for the transfer of personal information out of the EU, or improper processing of personal data under the GDPR. Failure by our collaborators to comply with the strict rules on the transfer of personal data outside the EU into the U.S. may result in the imposition of criminal and administrative sanctions on such collaborators or impact the flow of personal data outside the EU, which could adversely affect our business and could create liability for us.

Most U.S. health care providers, including research institutions from which we or our collaborators obtain clinical trial data, are subject to privacy and security regulations promulgated under HIPAA. For example, as part of our human genetics initiative, our wholly-owned subsidiary, Regeneron Genetics Center LLC, has entered into collaborations with research institutions, including the Geisinger Health System, which are subject to HIPAA. Regeneron is not a covered entity or business associate under HIPAA and thus is not subject to its requirements. However, we could be subject to criminal penalties if we, our affiliates, or our agents knowingly receive, use, or disclose PHI in a manner that is not permitted under HIPAA. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive PHI from a health care provider or research

institution that has not satisfied HIPAA's requirements for its disclosure. There are instances where we collect and maintain personal data, which may include health information that is outside the scope of HIPAA but within the scope of state health privacy laws or similar state level privacy legislation. This information may be received throughout the clinical trial process, in the course of our research collaborations, directly from individuals who enroll in our patient assistance programs, and from our own employees in a pandemic response process (such as in connection with the COVID-19 pandemic).

Consumer protection laws impact the manner in which we develop and maintain processes to support our patient assistance programs, product marketing activities, and the sharing of employee and clinical data for internal and third-party commercial activities. Several U.S. states have proposed and passed consumer privacy laws, which were modeled after the comprehensive consumer privacy law in California, the CCPA. The CCPA, which became effective on January 1, 2020, is a consumer protection law that establishes requirements for data use and sharing transparency and provides California residents with personal data privacy rights regarding the use, disclosure, and retention of their personal data. Amendments to the CCPA have, among other things, imposed new obligations to provide notice where personal data will be de-identified. These laws and regulations are constantly evolving and may impose limitations on our business activities. Several other U.S. states have introduced similar consumer protection laws that may go into effect in the near future. At the federal level, Section 5 of the Federal Trade Commission Act is a consumer protection law that bars unfair and deceptive acts and practices and requires, among other things, companies to notify individuals that they will safeguard their personal data and that they will fulfil the commitments made in their privacy notices. The Federal Trade Commission has brought legal actions against organizations that have violated consumers' privacy rights or have misled them by failing to maintain appropriate security.

Furthermore, health privacy laws, data breach notification laws, consumer protection laws, data localization laws, and genetic privacy laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use, and dissemination of individuals' health and other personal data. New state level genetic privacy and consumer protection laws in the United States may require additional transparency and permissions in our informed consent forms. Moreover, individuals about whom we or our collaborators obtain health or other personal data, as well as the providers and third parties who share this information with us, may have statutory or contractual limits that impact our ability to use and disclose the information. We are likely to be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws both inside and outside the United States. Many of these laws differ from each other in significant ways and have different effects. Many of the state laws enable a state attorney general to bring actions and provide private rights of action to consumers as enforcement mechanisms. Compliance with these laws requires a flexible privacy framework as they are constantly evolving. Failure to comply with these laws and regulations could result in government enforcement actions and create liability for us (which could include civil and/or criminal penalties), private litigation, and/or adverse publicity. Federal regulators, state attorneys general, and plaintiffs' attorneys have been active in this space. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or any collaborators fail to comply with applicable federal, state, local, or foreign regulatory requirements, we could be subject to a range of regulatory actions that could affect our or any collaborators' ability to commercialize our products and could harm, prevent, or substantially increase the cost of marketing and sales of any affected products that we are able to commercialize. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business.

Increasing use of social media could give rise to liability, breaches of data security, or reputational damage.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is a risk that the use of social media by us or our employees to communicate about our products or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our social media policy or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal data of our employees, clinical trial patients, customers, and others. Furthermore, negative posts or comments about us or our products in social media could seriously damage our reputation, brand image, and goodwill. Any of these events could have a material adverse effect on our business, prospects, operating results, and financial condition and could adversely affect the price of our Common Stock.

Risks Related to Our Reliance on Third Parties

If our Antibody Collaboration or our IO Collaboration with Sanofi is terminated, or Sanofi materially breaches its obligations thereunder, our business, prospects, operating results, and financial condition, and our ability to develop, manufacture, and commercialize certain of our products and product candidates in the time expected, or at all, would be materially harmed.

We rely on funding and support from Sanofi to develop, manufacture, and commercialize certain of our products and product candidates. With respect to the products that we are co-developing with Sanofi under our Antibody Collaboration (currently consisting of Dupixent, Kevzara, and itepekimab), Sanofi funds a significant portion of development expenses incurred in connection with the development of these products. In addition, we rely on Sanofi to lead much of the clinical development efforts, assist with or lead efforts to obtain and maintain regulatory approvals, and lead the commercialization efforts for these products and product candidates.

Under our IO Collaboration, Sanofi also funds half of the development expenses incurred in connection with the clinical development of Libtayo, subject to an agreed-upon development budget. We also rely on Sanofi to lead commercialization efforts outside the United States for Libtayo and to assist us to comply with the necessary requirements related to Libtayo's regulatory approvals in the EU.

If Sanofi terminates the Antibody Collaboration or the IO Collaboration or fails to comply with its payment obligations under any of our collaborations, our business, prospects, operating results, and financial condition would be materially harmed. We would be required to either expend substantially more resources than we have anticipated to support our research and development efforts, which could require us to seek additional funding that might not be available on favorable terms or at all, or materially cut back on such activities. If Sanofi does not perform its obligations with respect to the product candidates it is co-developing with us, our ability to develop, manufacture, and commercialize these product candidates will be significantly adversely affected. We have limited commercial capabilities outside the United States and would have to develop or outsource these capabilities for products commercialized under our Antibody Collaboration or our IO Collaboration (see also "Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *If we are unable to establish commercial capabilities outside the United States for products we intend to commercialize or co-commercialize outside the United States, our business, prospects, operating results, and financial condition may be adversely affected*" above). Termination of the Antibody Collaboration or the IO Collaboration would create substantial new and additional risks to the successful development and commercialization of the products subject to such collaborations, particularly outside the United States.

If our collaboration with Bayer for EYLEA is terminated, or Bayer materially breaches its obligations thereunder, our business, prospects, operating results, and financial condition, and our ability to continue to commercialize EYLEA outside the United States would be materially harmed.

We rely heavily on Bayer with respect to the commercialization of EYLEA outside the United States. Bayer is responsible for obtaining and maintaining regulatory approval outside the United States, as well as providing all sales, marketing, and commercial support for the product outside the United States. In particular, Bayer has responsibility for selling EYLEA outside the United States using its sales force and, in Japan, in cooperation with Santen pursuant to a Co-Promotion and Distribution Agreement, as in effect from time to time, with Bayer's Japanese affiliate. If Bayer and, in Japan, Santen do not perform their obligations in a timely manner, or at all, our ability to commercialize EYLEA outside the United States will be significantly adversely affected. Bayer has the right to terminate its collaboration agreement with us at any time upon six or twelve months' advance notice, depending on the circumstances giving rise to termination. If Bayer were to terminate its collaboration agreement with us, we may not have the resources or skills to replace those of our collaborator, which could require us to seek another collaboration that might not be available on favorable terms or at all, and could cause significant issues for the commercialization of EYLEA outside the United States and result in substantial additional costs and/or lower revenues to us. We have limited commercial capabilities outside the United States and would have to develop or outsource these capabilities (see also "Risks Related to Commercialization of Our Marketed Products, Product Candidates, and New Indications for Our Marketed Products - *If we are unable to establish commercial capabilities outside the United States for products we intend to commercialize or co-commercialize outside the United States, our business, prospects, operating results, and financial condition may be adversely affected*" above). Termination of the Bayer collaboration agreement would create substantial new and additional risks to the successful commercialization of EYLEA outside the United States.

Our collaborators and service providers may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of our drug candidates and current and future products.

We depend upon third-party collaborators, including Sanofi and Bayer, and service providers such as CROs, outside testing laboratories, clinical investigator sites, third-party manufacturers, fill/finish providers, and product packagers and labelers, to assist us in the manufacture and preclinical and clinical development of our product candidates. We also depend, or will depend,

on some of these third parties in connection with the commercialization of our marketed products and our product candidates and new indications for our marketed products if they are approved for marketing. If any of our existing collaborators or service providers breaches or terminates its agreement with us or does not perform its development or manufacturing services under an agreement in a timely manner (including as a result of its inability to perform due to financial or other relevant constraints) or in compliance with applicable GMPs, GLPs, or GCP standards, we could experience additional costs, delays, and difficulties in the manufacture or development of, or in obtaining approval by regulatory authorities for, or successfully commercializing our product candidates.

We and our collaborators rely on third-party service providers to support the distribution of our marketed products and for many other related activities in connection with the commercialization of these marketed products. Despite our or our collaborators' arrangements with them, these third parties may not perform adequately. If these service providers do not perform their services adequately, sales of our marketed products will suffer.

Risks Related to Employees

We are dependent on our key personnel and if we cannot recruit and retain leaders in our research, development, manufacturing, and commercial organizations, our business will be harmed.

We are highly dependent on certain of our executive officers, other key members of our senior management team, and the Chair of our board of directors. If we are not able to retain (or for any other reason lose the services of) any of these persons, our business may suffer. In particular, we depend on the services of P. Roy Vagelos, M.D., the Chair of our board of directors; Leonard S. Schleifer, M.D., Ph.D., our President and Chief Executive Officer; and George D. Yancopoulos, M.D., Ph.D., our President and Chief Scientific Officer. We are also highly dependent on the expertise and services of other senior management members leading our research, development, manufacturing, and commercialization efforts. There is intense competition in the biotechnology industry for qualified scientists and managerial personnel in the research, development, manufacture, and commercialization of drugs. We may not be able to continue to attract and retain the qualified personnel necessary to continue to advance our business and achieve our strategic objectives.

Information Technology Risks

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on critical, complex, and interdependent information technology systems, including Internet-based systems, to support business processes as well as internal and external communications. These systems are also critical to enable remote working arrangements, which have been growing in importance due in part to the COVID-19 pandemic and related developments. The size and complexity of our computer systems make us potentially vulnerable to IT system breakdowns, internal and external malicious intrusion, and computer viruses and ransomware, which may impact product production and key business processes. We also have outsourced significant elements of our information technology infrastructure and operations to third parties, which may allow them to access our confidential information and may also make our systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by such third parties or others.

In addition, our systems are potentially vulnerable to data security breaches - whether by employees or others - which may expose sensitive data to unauthorized persons. Data security breaches could lead to the loss of trade secrets or other intellectual property, result in demands for ransom or other forms of blackmail, or lead to the public exposure of personal information (including sensitive personal information) of our employees, clinical trial patients, customers, and others. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives (including industrial espionage or extortion) and expertise, including by organized criminal groups, "hacktivists," nation states, and others. As a company with an increasingly global presence, our systems are subject to frequent attacks. Due to the nature of some of these attacks, there is a risk that an attack may remain undetected for a period of time. While we continue to make investments to improve the protection of data and information technology, and to oversee and monitor the security measures of our suppliers and/or service providers, there can be no assurance that our efforts will prevent service interruptions or security breaches. In addition, we depend in part on third-party security measures over which we do not have full control to protect against data security breaches.

If we or our suppliers and/or service providers fail to maintain or protect our information technology systems and data security effectively, or fail to anticipate, plan for, or manage significant disruptions to these systems, we or our suppliers and/or service providers could have difficulty preventing, detecting, or controlling such disruptions or security breaches, which could result in legal proceedings, liability under laws that protect the privacy of personal information, disruptions to our operations, government investigations, breach of contract claims, and damage to our reputation, which could have a material adverse effect on our business, prospects, operating results, and financial condition.

Risks Related to Our Financial Results, Liquidity, and Need for Additional Financing

We may need additional funding in the future, which may not be available to us, and which may force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We expend substantial resources for research and development, including costs associated with clinical testing of our product candidates and new indications of our marketed products, the commercialization of products, and capital expenditures. We believe our existing capital resources and borrowing availability under our revolving credit facility, together with funds generated by our current and anticipated EYLEA net product sales and funding we are entitled to receive under our collaboration agreements and other similar agreements (including our share of profits in connection with commercialization of EYLEA and Dupixent under our collaboration agreements with Bayer and Sanofi, respectively), will enable us to meet our anticipated operating needs for the foreseeable future. However, one or more of our collaboration agreements may terminate, our revenues may fall short of our projections or be delayed, or our expenses may increase, any of which could result in our capital being consumed significantly faster than anticipated. Our expenses may increase for many reasons, including expenses in connection with the commercialization of our marketed products and the potential commercial launches of our product candidates and new indications for our marketed products, manufacturing scale-up, expenses related to clinical trials testing of antibody-based product candidates we are developing on our own (without a collaborator), and expenses for which we are responsible in accordance with the terms of our collaboration agreements.

We cannot be certain that our existing capital resources and our current and anticipated revenues will be sufficient to meet our operating needs. We may require additional financing in the future and we may not be able to raise additional funds on acceptable terms or at all. For example, there is no guarantee that we will have the ability to pay the principal amount due on our senior unsecured notes at maturity or redeem, repurchase, or refinance the notes prior to maturity on acceptable terms or at all. In addition, in March 2017, we completed a $720.0 million lease financing for our existing corporate headquarters and other rentable area consisting of approximately 150 acres of predominately office buildings and laboratory space located in Tarrytown, New York. In September 2021, we delivered a request to the lease financing participants to potentially exercise the option for a five-year extension of the term of the lease and the maturity date under the related participation agreement; and in November 2021, the lease financing participants consented to such extension, subject to the satisfaction of certain conditions prior to the expiration of the existing term in March 2022. There can be no assurance that such extension will become effective on favorable terms or at all. If such extension does not become effective, we would be obligated to purchase the facility by the end of the existing term in March 2022 by paying a purchase price of $720.0 million, together with all accrued and unpaid interest and yield and all other outstanding amounts under the relevant documents. Refer to Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources - *Tarrytown, New York Leases*" for further details. Our ability to refinance or to obtain additional financing could be adversely affected if there is a significant decline in the demand for our products or other significantly unfavorable changes in economic conditions. Volatility in the financial markets could increase borrowing costs or affect our ability to raise capital. If additional financing is necessary and we obtain it through the sale of equity securities, such sales will likely be dilutive to our shareholders. Debt financing arrangements may require us to pledge certain assets or enter into covenants that would restrict our business activities or our ability to incur further indebtedness and may be at interest rates and contain other terms that are not favorable to our shareholders. Should we require and be unable to raise sufficient funds (i) to complete the development of our product candidates, (ii) to successfully commercialize our product candidates or new indications for our marketed products if they obtain regulatory approval, and (iii) to continue our manufacturing and marketing of our marketed products, we may face delay, reduction, or elimination of our research and development or preclinical or clinical programs and our commercialization activities, which would significantly limit our potential to generate revenue.

Our indebtedness could adversely impact our business.

We have certain indebtedness and contingent liabilities, including milestone and royalty payment obligations. As of December 31, 2021, we had an aggregate of $2.700 billion of outstanding indebtedness under our senior unsecured notes and the lease financing facility. We may also incur additional debt in the future. Any such indebtedness could:

- limit our ability to access capital markets and incur additional debt in the future;
- require us to dedicate a substantial portion of our cash flow from operations to payments on our indebtedness, thereby reducing the availability of our cash flow for other purposes, including business development efforts, research and development, and mergers and acquisitions; and
- limit our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate, thereby placing us at a competitive disadvantage compared to competitors that have less debt.

Changes in foreign currency exchange rates could have a material adverse effect on our operating results.

Our revenue from outside the United States will increase as our products, whether marketed or otherwise commercialized by us or our collaborators, gain marketing approval in such jurisdictions. Our primary foreign currency exposure relates to movements in the Japanese yen, euro, British pound sterling, Canadian dollar, and Australian dollar. If the U.S. dollar weakens against a specific foreign currency, our revenues will increase, having a positive impact on net income, but our overall expenses will increase, having a negative impact. Conversely, if the U.S. dollar strengthens against a specific foreign currency, our revenues will decrease, having a negative impact on net income, but our overall expenses will decrease, having a positive impact. Therefore, significant changes in foreign exchange rates can impact our operating results and the financial condition of our Company.

Our investments are subject to risks and other external factors that may result in losses or affect the liquidity of these investments.

As of December 31, 2021, we had $2.886 billion in cash and cash equivalents and $9.647 billion in marketable securities (including $1.250 billion in equity securities). Our investments consist primarily of debt securities, including investment-grade corporate bonds. These fixed-income investments are subject to external factors that may adversely affect their market value or liquidity, such as interest rate, liquidity, market, and issuer credit risks, including actual or anticipated changes in credit ratings. The equity securities we hold may experience significant volatility and may decline in value or become worthless if the issuer experiences an adverse development. Furthermore, our equity investments could be subject to dilution (and decline in value) as a result of the issuance of additional equity interests by the applicable issuer. If any of our investments suffer market price declines, such declines may have an adverse effect on our financial condition and operating results.

Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect our business, operating results, and financial condition.

We are subject to risks related to uncertainty regarding the London Interbank Offered Rate ("LIBOR"), which is in the process of being phased out. The U.K. Financial Conduct Authority, which regulates LIBOR, has announced that it intends to phase out LIBOR. The publication of U.S. dollar LIBOR for certain tenors and all non-U.S. dollar LIBOR tenors ceased after December 31, 2021 (other than certain sterling and Japanese yen settings being published on a synthetic temporary basis). Banks reporting information used to set U.S. dollar LIBOR for all other tenors are currently expected to stop doing so after June 30, 2023, although the LIBOR administrator may discontinue or modify LIBOR prior to that date. In 2021, the U.S. Federal Reserve Board and certain other regulatory bodies issued guidance encouraging banks and other financial market participants to cease entering into new contracts that use U.S. dollar LIBOR as a reference rate as soon as practicable and in any event no later than December 31, 2021. Although regulators in various jurisdictions have been working to replace LIBOR and have encouraged the development and adoption of alternative reference rates, such as the Secured Overnight Financing Rate ("SOFR"), there continues to be uncertainty regarding the nature of potential changes to and future utilization of specific LIBOR tenors, the development and acceptance of alternative reference rates, and other reforms. We cannot predict the consequences and timing of these developments or other market or regulatory changes related to the phase-out of LIBOR. A transition away from LIBOR as a benchmark for establishing the applicable interest rate may adversely affect our outstanding variable-rate indebtedness (if any) and our variable-rate finance lease, as well as floating-rate debt securities in our investment portfolio. For example, if a published U.S. dollar LIBOR is unavailable or no longer representative, interest for borrowings (if any) with an interest rate based on LIBOR under our revolving credit facility will be determined using various alternative methods, any of which may result in interest obligations which are more than, or do not otherwise correlate over time with, the payments that would have been made on such debt prior to any LIBOR phase-out.

Risks Related to Our Common Stock

Our stock price is extremely volatile.

There has been significant volatility in our stock price and generally in the market prices of biotechnology companies' securities. Various factors and events may have a significant impact on the market price of our Common Stock. These factors include, by way of example:

- net product sales of our marketed products (as recorded by us or our collaborators), in particular EYLEA, Dupixent, and Libtayo, as well as our overall operating results;
- if any of our product candidates or our new indications for our marketed products receive regulatory approval, net product sales of, and profits from, these product candidates and new indications;
- market acceptance of, and the market share for, our marketed products, especially EYLEA, Dupixent, and Libtayo;
- whether our net product sales and net profits underperform, meet, or exceed the expectations of investors or analysts;
- announcement of actions by the FDA or foreign regulatory authorities or their respective advisory committees regarding our, or our collaborators', or our competitors', currently pending or future application(s) for regulatory approval of product candidate(s) or new indications for marketed products;
- announcement of submission of an application for regulatory approval of one or more of our, or our competitors', product candidates or new indications for marketed products;
- progress, delays, or results in clinical trials of our or our competitors' product candidates or new indications for marketed products;
- impact of the COVID-19 pandemic on our business, including future sales of REGEN-COV;
- announcement of technological innovations or product candidates by us or competitors;
- claims by others that our products or technologies infringe their patents;
- challenges by others to our patents in the EPO and in the USPTO;
- public concern as to the safety or effectiveness of any of our marketed products or product candidates or new indications for our marketed products;
- pricing or reimbursement actions, decisions, or recommendations by government authorities, insurers, or other organizations (such as health maintenance organizations and PBMs) affecting the coverage, reimbursement, or use of any of our marketed products or competitors' products;
- our ability to raise additional capital as needed on favorable terms;
- developments in our relationships with collaborators or key customers;
- developments in the biotechnology industry or in government regulation of healthcare, including those relating to compounding (i.e., a practice in which a pharmacist, a physician, or, in the case of an outsourcing facility, a person under the supervision of a pharmacist, combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient);
- large sales of our Common Stock by our executive officers or other employees, directors, or significant shareholders (or the expectation of any such sales);
- changes in tax rates, laws, or interpretation of tax laws;
- arrivals and departures of key personnel;
- general market conditions;
- our ability to repurchase our Common Stock under any share repurchase program on favorable terms or at all;
- trading activity that results from the rebalancing of stock indices in which our Common Stock is included, or the inclusion or exclusion of our Common Stock from such indices;
- other factors identified in these "Risk Factors"; and
- the perception by the investment community or our shareholders of any of the foregoing factors.

The trading price of our Common Stock has been, and could continue to be, subject to wide fluctuations in response to these and other factors, including the sale or attempted sale of a large amount of our Common Stock in the market. As discussed in greater detail under "*Future sales of our Common Stock by our significant shareholders or us may depress our stock price and impair our ability to raise funds in new share offerings*" below, a large percentage of our Common Stock is owned by a small number of our principal shareholders. As a result, the public float of our Common Stock (i.e., the portion of our Common Stock held by public investors, as opposed to the Common Stock held by our directors, officers, and principal shareholders) may be lower than the public float of other large public companies with broader public ownership. Therefore, the trading price of our Common Stock may fluctuate significantly more than the stock market as a whole. These factors may exacerbate the volatility in the trading price of our Common Stock and may negatively impact your ability to liquidate your investment in Regeneron at the time you wish at a price you consider satisfactory. Broad market fluctuations may also adversely affect the market price of our Common Stock. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also

require us to make substantial payments to satisfy judgments or to settle litigation, which may harm our business, prospects, operating results, and financial condition.

Future sales of our Common Stock by our significant shareholders or us may depress our stock price and impair our ability to raise funds in new share offerings.

A small number of our shareholders beneficially own a substantial amount of our Common Stock. As of December 31, 2021, our five largest shareholders plus Dr. Schleifer, our Chief Executive Officer, beneficially owned approximately 38.1% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of December 31, 2021. If our significant shareholders or we sell substantial amounts of our Common Stock in the public market, or there is a perception that such sales may occur, the market price of our Common Stock could fall. Sales of Common Stock by our significant shareholders also might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

There can be no assurance that we will repurchase shares of our Common Stock or that we will repurchase shares at favorable prices.

In November 2021, our board of directors authorized a share repurchase program to repurchase up to $3.0 billion of our Common Stock (of which $2.845 billion remained available as of December 31, 2021). There can be no assurance of any future share repurchases or share repurchase program authorizations. Any share repurchases will depend upon, among other factors, our cash balances and potential future capital requirements, our results of operations and financial condition, the price of our Common Stock on the NASDAQ Global Select Market, and other factors that we may deem relevant. We can provide no assurance that we will repurchase shares of our Common Stock at favorable prices, if at all.

Our existing shareholders may be able to exert substantial influence over matters requiring shareholder approval and over our management.

Holders of Class A Stock, who are generally the shareholders who purchased their stock from us before our initial public offering, are entitled to ten votes per share, while holders of Common Stock are entitled to one vote per share. As of December 31, 2021, holders of Class A Stock held 14.6% of the combined voting power of all shares of Common Stock and Class A Stock then outstanding. These shareholders, if acting together, would be in a position to substantially influence the election of our directors and the vote on certain corporate transactions that require majority or supermajority approval of the combined classes, including mergers and other business combinations. This may result in our taking corporate actions that other shareholders may not consider to be in their best interest and may affect the price of our Common Stock. As of December 31, 2021:

- our current executive officers and directors beneficially owned 7.4% of our outstanding shares of Common Stock, assuming conversion of their Class A Stock into Common Stock and the exercise of all options held by such persons which are exercisable within 60 days of December 31, 2021, and 18.8% of the combined voting power of our outstanding shares of Common Stock and Class A Stock, assuming the exercise of all options held by such persons which are exercisable within 60 days of December 31, 2021; and
- our five largest shareholders plus Dr. Schleifer, our Chief Executive Officer, beneficially owned approximately 38.1% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of December 31, 2021. In addition, these five shareholders plus our Chief Executive Officer held approximately 45.4% of the combined voting power of our outstanding shares of Common Stock and Class A Stock, assuming the exercise of all options held by our Chief Executive Officer which are exercisable within 60 days of December 31, 2021.

The anti-takeover effects of provisions of our charter, by-laws, and of New York corporate law, as well as the contractual provisions in our investor and collaboration agreements and certain provisions of our compensation plans and agreements, could deter, delay, or prevent an acquisition or other "change of control" of us and could adversely affect the price of our Common Stock.

Our certificate of incorporation, our by-laws, and the New York Business Corporation Law contain various provisions that could have the effect of delaying or preventing a change in control of our Company or our management that shareholders may consider favorable or beneficial. Some of these provisions could discourage proxy contests and make it more difficult for shareholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our Common Stock. These provisions include:

- authorization to issue "blank check" preferred stock, which is preferred stock that can be created and issued by the board of directors without prior shareholder approval, with rights senior to those of our Common Stock and Class A Stock;
- a staggered board of directors, so that it would take three successive annual shareholder meetings to replace all of our directors;
- a requirement that removal of directors may only be effected for cause and only upon the affirmative vote of at least eighty percent (80%) of the outstanding shares entitled to vote for directors, as well as a requirement that any vacancy on the board of directors may be filled only by the remaining directors;
- a provision whereby any action required or permitted to be taken at any meeting of shareholders may be taken without a meeting, only if, prior to such action, all of our shareholders consent, the effect of which is to require that shareholder action may only be taken at a duly convened meeting;
- a requirement that any shareholder seeking to bring business before an annual meeting of shareholders must provide timely notice of this intention in writing and meet various other requirements; and
- under the New York Business Corporation Law, in addition to certain restrictions which may apply to "business combinations" involving our Company and an "interested shareholder," a plan of merger or consolidation of our Company must be approved by two-thirds of the votes of all outstanding shares entitled to vote thereon. See the risk factor above captioned "*Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval and over our management.*"

Further, Sanofi, Bayer, and Teva are currently bound by certain "standstill" provisions under the January 2014 amended and restated investor agreement between us and Sanofi, as amended; our 2016 ANG2 license and collaboration agreement and our 2014 PDGFR-beta license and collaboration agreement with Bayer; and our 2016 collaboration agreement with Teva, respectively. These provisions contractually prohibit Sanofi, Bayer, and Teva from seeking to directly or indirectly exert control of our Company or acquiring more than a specified percentage of our Class A Stock and Common Stock, taken together (30% in the case of Sanofi, 20% in the case of Bayer, and 5% in the case of Teva).

In addition, our Change in Control Severance Plan and the employment agreement with our Chief Executive Officer, each as amended and restated, provide for severance benefits in the event of termination as a result of a change in control of our Company. Also, equity awards issued under our long-term incentive plans may become fully vested in connection with a "change in control" of our Company, as defined in the plans. These contractual provisions may also have the effect of deterring, delaying, or preventing an acquisition or other change in control.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We conduct our research, development, manufacturing, and administrative activities at our owned and leased facilities. A summary of our significant owned and leased properties is provided below.

Tarrytown, New York

At our Tarrytown, New York location, we lease approximately 1,467,000 square feet of laboratory and office space, of which approximately 1,354,000 square feet is occupied by Regeneron. Refer to Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources - *Tarrytown, New York Leases*" for further details. We also own an approximate 100-acre parcel of undeveloped land adjacent to our Tarrytown, New York location, which we plan to start developing in 2022, primarily in connection with expanding our research and support facilities to accommodate our growth.

Rensselaer, New York

We own facilities in Rensselaer, New York totaling approximately 950,000 square feet of manufacturing, research, office, and warehouse space. This includes approximately 212,000 square feet of warehouse space which we constructed on a 130-acre parcel of land near our Rensselaer facility. We are in the process of further developing this property, primarily in connection with constructing a fill/finish facility.

Limerick, Ireland

We own a facility in Limerick, Ireland totaling approximately 555,000 square feet of manufacturing, warehouse, laboratory, and office space. We are in the process of further developing this property to support our growth and expand our manufacturing capacity.

ITEM 3. LEGAL PROCEEDINGS

The information called for by this item is incorporated herein by reference to the information set forth in Note 15 to our Consolidated Financial Statements included in this report.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES

Market for Registrant's Common Equity

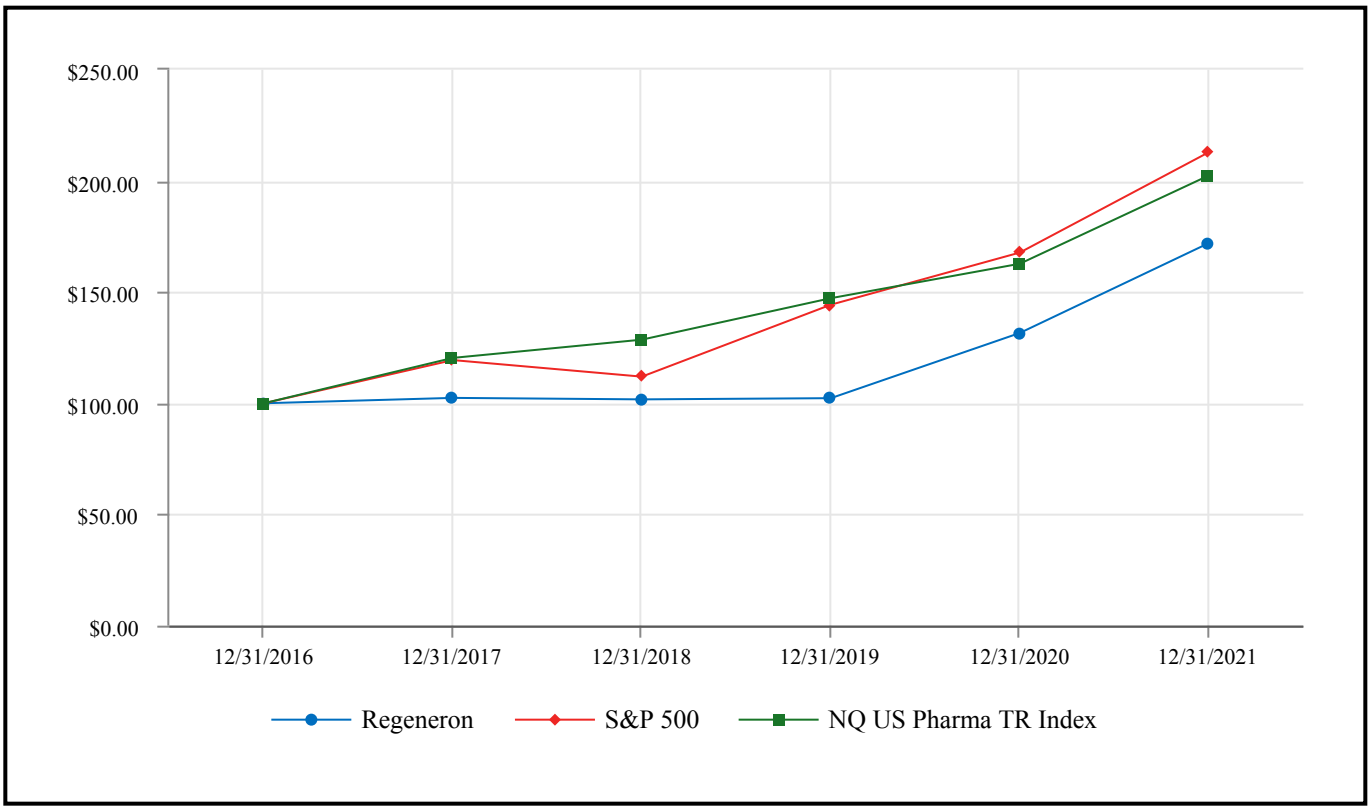
Our Common Stock, par value $.001 per share, is quoted on The NASDAQ Global Select Market under the symbol "REGN." Our Class A Stock, par value $.001 per share, is not publicly quoted or traded.

As of January 27, 2022, there were 166 shareholders of record of our Common Stock and 15 shareholders of record of our Class A Stock.

We have never paid cash dividends on our Common Stock or Class A Stock and do not anticipate paying any in the foreseeable future.

STOCK PERFORMANCE GRAPH

Set forth below is a line graph comparing the cumulative total shareholder return on Regeneron's Common Stock with the cumulative total return of (i) the NASDAQ US Benchmark Pharmaceuticals Total Return Index ("NQ US Pharma TR Index"), and (ii) Standard & Poor's 500 Stock Index ("S&P 500") for the period from December 31, 2016 through December 31, 2021. The comparison assumes that $100 was invested on December 31, 2016 in our Common Stock and in both of the foregoing indices. All values assume reinvestment of the pre-tax value of dividends paid by companies included in these indices. The historical stock price performance of our Common Stock shown in the graph below is not necessarily indicative of future stock price performance.



	12/31/2016	12/31/2017	12/31/2018	12/31/2019	12/31/2020	12/31/2021
Regeneron	$ 100.00	$ 102.42	$ 101.75	$ 102.29	$ 131.61	$ 172.03
S&P 500	$ 100.00	$ 119.42	$ 111.97	$ 144.31	$ 167.77	$ 212.89
NQ US Pharma TR Index	$ 100.00	$ 120.40	$ 128.60	$ 147.25	$ 162.74	$ 202.43

This performance graph shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or incorporated by reference into any filing of ours under the Securities Act of 1933, as amended, or the Securities Exchange Act, except as shall be expressly set forth by specific reference to such filing.

Issuer Purchases of Equity Securities

The table below reflects shares of Common Stock we repurchased under our share repurchase programs, as well as Common Stock withheld by us for employees to satisfy their tax withholding obligations arising upon the vesting of restricted stock granted under one of our long-term incentive plans, during the three months ended December 31, 2021. Refer to Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources" for further details of our share repurchase programs.

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Programs	Approximate Dollar Value of Shares that May Yet Be Purchased Under the Programs *(in millions)*
10/1/2021–10/31/2021	1,195,053	$ 560.51	1,195,053	$ 27.5
11/1/2021–11/30/2021	110,500	$ 645.90	110,500	$ 2,956.1 [(b)]
12/1/2021–12/31/2021	271,289	$ 643.03	176,000	$ 2,845.0
Total	1,576,842 [(a)]		1,481,553 [(a)]	

[(a)] The difference between the total number of shares purchased and the total number of shares purchased as part of publicly announced programs relates to Common Stock withheld by us for employees to satisfy their tax withholding obligations arising upon the vesting of restricted stock granted under one of our long-term incentive plans.

[(b)] In November 2021, our board of directors authorized an additional share repurchase program to repurchase up to $3.0 billion of our Common Stock.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion should be read in conjunction with the consolidated financial statements and related notes included elsewhere in this report. Refer to Part II, Item 7 in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 (filed with the SEC on February 8, 2021) for additional discussion of our financial condition and results of operations for the year ended December 31, 2019, as well as our financial condition and results of operations for the year ended December 31, 2020 compared to the year ended December 31, 2019.

Overview

Regeneron Pharmaceuticals, Inc. is a fully integrated biotechnology company that discovers, invents, develops, manufactures, and commercializes medicines for serious diseases. Our commercialized medicines and product candidates in development are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematologic conditions, infectious diseases, and rare diseases.

We currently have nine FDA-approved products that have received marketing approval and over 30 product candidates in clinical development, almost all of which were homegrown in our laboratories. In addition, REGEN-COV has not been approved by the FDA, but has been authorized under an EUA for COVID-19 (see Part I, Item 1. "Business - REGEN-COV - Emergency and Temporary Use Authorizations" for a description of recent revisions to the EUA to exclude its use in geographic regions where infection or exposure is likely due to a variant that is not susceptible to the treatment). Also refer to Part I, Item 1. "Business - Products" and "Business - Programs in Clinical Development" for additional information related to marketed products and product candidates.

Our ability to generate profits and to generate positive cash flow from operations over the next several years depends significantly on the continued success in commercializing EYLEA and Dupixent. We expect to continue to incur substantial expenses related to our research and development activities, a portion of which we expect to be reimbursed by our collaborators. Also, our research and development activities outside our collaborations, the costs of which are not reimbursed, are expected to expand and require additional resources. We also expect to incur substantial costs related to the commercialization of our marketed products. Our financial results may fluctuate from quarter to quarter and will depend on, among other factors, the net sales of our products; the scope and progress of our research and development efforts; the timing of certain expenses; the continuation of our collaborations, in particular with Sanofi and Bayer, including our share of collaboration profits or losses from sales of products and the amount of reimbursement of our research and development expenses that we receive from collaborators; and the amount of income tax expense we incur, which is partly dependent on the profits or losses we earn in each of the countries in which we operate. We cannot predict whether or when new products or new indications for marketed products will receive regulatory approval or, if any such approval is received, whether we will be able to successfully commercialize such product(s) and whether or when they may become profitable.

Critical Accounting Policies and Use of Estimates

A summary of the significant accounting policies that impact us is provided in Note 1 to our Consolidated Financial Statements. The preparation of financial statements in accordance with accounting principles generally accepted in the United States of America ("GAAP") requires management to make estimates and assumptions that affect reported amounts and related disclosures in the financial statements. Management considers an accounting estimate to be critical if:

- it requires an assumption (or assumptions) regarding a future outcome; and
- changes in the estimate or the use of different assumptions to prepare the estimate could have a material effect on our results of operations or financial condition.

Management believes the current assumptions used to estimate amounts reflected in our Consolidated Financial Statements are appropriate. However, if actual experience differs from the assumptions used in estimating amounts reflected in our Consolidated Financial Statements, the resulting changes could have a material adverse effect on our results of operations, and, in certain situations, could have a material adverse effect on our liquidity and financial condition. The critical accounting estimates that impact our Consolidated Financial Statements are described below.

Revenue Recognition - Product Revenue

We recognize revenue from product sales at a point in time when our customer is deemed to have obtained control of the product, which generally occurs upon receipt or acceptance by our customer.

The amount of revenue we recognize from product sales may vary due to rebates, chargebacks, and discounts provided under governmental and other programs, distribution-related fees, and other sales-related deductions. In order to determine the transaction price, we estimate, utilizing the expected value method, the amount of variable consideration to which we will be entitled. This estimate is based upon contracts with customers, healthcare providers, payors and government agencies, statutorily-defined discounts applicable to government-funded programs, historical experience, estimated payor mix, and other relevant factors. Calculating these provisions involves estimates and judgments. We review our estimates of rebates, chargebacks, and other applicable provisions each period and record any necessary adjustments in the current period's net product sales. Refer to the "Results of Operations - *Revenues - Net Product Sales*" section below for further details regarding our provisions, and credits/payments, for sales-related deductions.

Collaborative Arrangements

We have entered into various collaborative arrangements to research, develop, manufacture, and commercialize products and/or product candidates.

Our collaboration agreements may require us to deliver various rights, services, and/or goods across the entire life cycle of a product or product candidate. In agreements involving multiple goods or services promised to be transferred to our collaborator, we must assess, at the inception of the contract, whether each promise represents a separate obligation (i.e., is "distinct"), or whether such promises should be combined as a single unit of account. When we have a combined unit of account which includes a license and providing research and development services to our collaborator, recognition of up-front payments and development milestones earned from our collaborator is deferred (as a liability) and recognized over the development period (i.e., over time). In arrangements where we satisfy our obligation(s) during the development phase over time, we recognize amounts initially deferred over time typically using an input method on the basis of our research and development costs incurred relative to the total expected cost which determines the extent of our progress toward completion. We review our estimates each period and make revisions to such estimates as necessary. Due to the variability in the scope of activities and length of time necessary to develop a drug product, potential delays in development programs, changes to development plans and budgets as programs progress, including if we and our collaborators decide to expand or contract our clinical plans for a drug candidate in various disease indications, and uncertainty in the ultimate requirements to obtain governmental approval for commercialization, revisions to our estimates are likely to occur periodically, potentially resulting in material changes to amounts recognized.

When we are entitled to reimbursement of all or a portion of the expenses (e.g., research and development expenses) that we incur under a collaboration, we record those reimbursable amounts in the period in which such costs are incurred.

If our collaborator performs research and development work or commercialization-related activities and share costs, we also recognize, as expense (e.g., research and development expense or selling, general and administrative expense, as applicable) in the period when our collaborator incurs such expenses, the portion of the collaborator's expenses that we are obligated to reimburse. Our collaborators provide us with estimated expenses for the most recent fiscal quarter. The estimates are revised, if necessary, in subsequent periods if actual expenses differ from those estimates.

Under certain of the Company's collaboration agreements, product sales and cost of sales may be recorded by the Company's collaborators as they are deemed to be the principal in the transaction. In arrangements where we:

- supply commercial product to our collaborator, we may be reimbursed for our manufacturing costs as commercial product is shipped to the collaborator; however, recognition of such cost reimbursements may be deferred until the product is sold by our collaborator to third-party customers;
- share in any profits or losses arising from the commercialization of such products, we record our share of the variable consideration, representing net product sales less cost of goods sold and shared commercialization and other expenses, in the period in which such underlying sales occur and costs are incurred by the collaborator; and
- receive royalties and/or sales-based milestone payments from our collaborator, we recognize such amounts in the period earned.

Our collaborators provide us with estimates of product sales and our share of profits or losses, as applicable, for each quarter. The estimates are revised, if necessary, in subsequent periods if our share of actual profits or losses differ from those estimates.

Stock-based Compensation

We recognize stock-based compensation expense for equity grants under our long-term incentive plans to employees and non-employee members of our board of directors based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period.

We use the Black-Scholes model to compute the estimated fair value of stock option awards. Using this model, fair value is calculated based on assumptions with respect to (i) expected volatility of our Common Stock price, (ii) the periods of time over

which employees and members of our board of directors are expected to hold their options prior to exercise (expected lives), (iii) expected dividend yield on our Common Stock, and (iv) risk-free interest rates, which are based on quoted U.S. Treasury rates for securities with maturities approximating the options' expected lives. Expected volatility has been estimated based on actual movements in our stock price over the most recent historical periods equivalent to the options' expected lives. Expected lives are principally based on our historical exercise experience with previously issued employee and board of director option grants. The expected dividend yield is zero as we have never paid dividends and do not currently anticipate paying any in the foreseeable future.

Stock-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

We use a Monte Carlo simulation to compute the estimated fair value of performance-based restricted stock units, which are subject to vesting based on the Company's attainment of pre-established market performance goals.

The assumptions used in computing the fair value of equity awards reflect our best estimates but involve uncertainties related to market and other conditions, many of which are outside of our control. Changes in any of these assumptions may materially affect the fair value of awards granted and the amount of stock-based compensation recognized in future periods.

Income Taxes

We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns, including deferred tax assets and liabilities for expected amounts of global intangible low-taxed income ("GILTI") inclusions. Deferred tax assets and liabilities are determined as the difference between the tax basis of assets and liabilities and their respective financial reporting amounts ("temporary differences") at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on all available evidence, including scheduled reversals of deferred tax liabilities, projected future taxable income, tax planning strategies, results of recent operations, and our historical earnings experience by taxing jurisdiction. Significant judgment is required in making this assessment.

Uncertain tax positions, for which management's assessment is that there is more than a 50% probability that the position will be sustained upon examination by a taxing authority based upon its technical merits, are subjected to certain recognition and measurement criteria. Significant judgment is required in making this assessment, and, therefore, we re-evaluate uncertain tax positions and consider various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, and changes in facts or circumstances related to a tax position. We adjust the amount of the liability to reflect any subsequent changes in the relevant facts and circumstances surrounding the uncertain positions.

Inventories

We capitalize inventory costs associated with our products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns, potential labeling restrictions, and any other impediments to obtaining regulatory approval.

We periodically analyze our inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, and write down such inventories as appropriate. In addition, our products are subject to strict quality control and monitoring which we perform throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, we record a charge to write down such inventory to its estimated realizable value.

See Note 6 to our Consolidated Financial Statements for information related to our inventory write-offs and reserves.

Contingencies

We accrue, based on management's judgment, for an estimated loss when the potential loss from claims or legal proceedings is considered probable and the amount can be reasonably estimated. As additional information becomes available, or, based on specific events such as the outcome of litigation or settlement of claims, we reassess the potential liability related to pending claims and litigation, and may change our estimates.

Results of Operations

Net Income

(In millions, except per share data)	Year Ended December 31, 2021	2020	2019
Revenues	$ 16,071.7	$ 8,497.1	$ 6,557.6
Operating expenses	7,124.9	4,920.5	4,347.8
Income from operations	8,946.8	3,576.6	2,209.8
Other income (expense)	379.0	233.8	219.3
Income before income taxes	9,325.8	3,810.4	2,429.1
Income tax expense	1,250.5	297.2	313.3
Net income	$ 8,075.3	$ 3,513.2	$ 2,115.8
Net income per share - diluted	$ 71.97	$ 30.52	$ 18.46

Revenues

(In millions)	Year Ended December 31, 2021	2020	2019	$ Change 2021 vs. 2020	2020 vs. 2019
Net product sales in the United States:					
EYLEA	$ 5,792.3	$ 4,947.2	$ 4,644.2	$ 845.1	$ 303.0
Libtayo	306.3	270.7	175.7	35.6	95.0
Praluent	170.0	150.9 *	*	*	*
REGEN-COV	5,828.0	185.7	—	5,642.3	185.7
Evkeeza	18.4	—	—	18.4	—
ARCALYST	2.2 **	13.1	14.5	**	(1.4)
Collaboration revenue:					
Sanofi	1,902.2	1,186.4	403.6	715.8	782.8
Bayer	1,409.3	1,186.1	1,145.6	223.2	40.5
Roche	361.8	—	—	361.8	—
Other revenue	281.2	557.0	174.0	(275.8)	383.0
Total revenues	$ 16,071.7	$ 8,497.1	$ 6,557.6	$ 7,574.6	$ 1,939.5

* Net product sales of Praluent in the United States were recorded by Sanofi prior to April 1, 2020.

** Effective April 1, 2021, Kiniksa records net product sales of ARCALYST in the United States.

Net Product Sales

Net product sales of EYLEA in the United States increased in 2021, compared to 2020, due to higher sales volume (including the adverse impact of the COVID-19 pandemic on U.S. EYLEA demand during the three months ended June 30, 2020), partly offset by an increase in sales-related deductions.

During the years ended December 31, 2021 and 2020, net product sales of REGEN-COV were recorded in connection with our agreements with the U.S. government. As of December 31, 2021, the Company had completed its final deliveries of drug product under its agreements with the U.S. government. Refer to Part I, Item 1. "Business - Agreements Related to COVID-19 - *U.S. Government*" for further details. The degree to which future sales of our COVID-19 monoclonal antibodies will continue is highly uncertain and will depend on, among other factors, the number of new COVID-19 cases and effectiveness of our product against variants of concern. Refer to Part I, Item 1. "Business - Products - REGEN-COV - Emergency and Temporary Use Authorizations" for additional information.

Revenue from product sales is recorded net of applicable provisions for rebates, chargebacks, and discounts; distribution-related fees; and other sales-related deductions. The following table summarizes the provisions, and credits/payments, for sales-related deductions.

(In millions)	Rebates, Chargebacks, and Discounts	Distribution-Related Fees	Other Sales-Related Deductions	Total
Balance as of December 31, 2018	$ 41.1	$ 42.0	$ 8.3	$ 91.4
Provisions	423.2	242.9	61.8	727.9
Credits/payments	(384.0)	(238.5)	(40.7)	(663.2)
Balance as of December 31, 2019	80.3	46.4	29.4	156.1
Provisions	762.9	279.9	94.1	1,136.9
Credits/payments	(641.0)	(249.1)	(78.7)	(968.8)
Balance as of December 31, 2020	202.2	77.2	44.8	324.2
Provisions	1,047.1	363.6	150.4	1,561.1
Credits/payments	(1,034.7)	(360.8)	(127.6)	(1,523.1)
Balance as of December 31, 2021	$ 214.6	$ 80.0	$ 67.6	$ 362.2

Sanofi Collaboration Revenue

	Year Ended December 31,		
(In millions)	2021	2020	2019
Antibody:			
Regeneron's share of profits in connection with commercialization of antibodies	$ 1,363.0	$ 785.2	$ 209.3
Sales-based milestones earned	50.0	50.0	—
Reimbursement for manufacturing of commercial supplies[(1)]	488.8	368.0	216.0
Total Antibody	1,901.8	1,203.2	425.3
Immuno-oncology:			
Regeneron's share of losses in connection with commercialization of Libtayo outside the United States	(13.6)	(25.7)	(21.7)
Reimbursement for manufacturing of commercial supplies[(1)]	14.0	8.9	—
Total Immuno-oncology	0.4	(16.8)	(21.7)
Total Sanofi collaboration revenue	$ 1,902.2	$ 1,186.4	$ 403.6

[(1)] Corresponding costs incurred by us in connection with such production is recorded within Cost of collaboration and contract manufacturing

Antibody

The increase in our share of profits in connection with commercialization of antibodies in 2021, compared to 2020, was driven by higher Dupixent profits.

During each of the years ended December 31, 2021 and 2020, the Company earned $50.0 million sales-based milestones from Sanofi, upon aggregate annual sales of antibodies outside the United States (including Praluent) exceeding $1.5 billion and $1.0 billion, respectively, on a rolling twelve-month basis. We are entitled to receive up to an aggregate of $150.0 million in additional milestone payments from Sanofi, which includes the next sales milestone payment of $50.0 million that would be earned when such sales outside the United States exceed $2.0 billion on a rolling twelve-month basis.

The increase in reimbursements for manufacturing of commercial supplies in 2021, compared to 2020, was primarily due to higher Dupixent sales, as revenue for such cost reimbursements is recognized when the product is sold by Sanofi to third-party customers.

Regeneron's share of profits in connection with the commercialization of Dupixent, Praluent (through March 31, 2020), and Kevzara is summarized below:

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
Dupixent, Praluent, and Kevzara net product sales[(1)]	$ 6,536.3	$ 4,394.5	$ 2,811.0
Regeneron's share of collaboration profits	1,511.5	871.5	233.0
Reimbursement of development expenses incurred by Sanofi in accordance with Regeneron's payment obligation	(148.5)	(86.3)	(23.7)
Regeneron's share of profits in connection with commercialization of antibodies	$ 1,363.0	$ 785.2	$ 209.3
Regeneron's share of collaboration profits as a percentage of Dupixent, Praluent, and Kevzara net product sales	21%	18%	7%

(1) Global net product sales of Dupixent and Kevzara are recorded by Sanofi. The quarter ended March 31, 2020 was the last quarter for which Sanofi and the Company shared profits and losses in connection with Sanofi's global net sales and the related commercialization of Praluent (see further details below); therefore, the quarter ended March 31, 2020 was the last quarter for which net product sales of Praluent were included in the table above.

As described in Part I, Item 1. "Business - Collaboration, License, and Other Agreements - Sanofi - Antibody", effective April 1, 2020, the Company became solely responsible for the development and commercialization of Praluent in the United States. Under the new agreement, Sanofi is solely responsible for the development and commercialization of Praluent outside of the United States, and pays the Company a 5% royalty on Sanofi's net product sales of Praluent outside the United States.

Bayer Collaboration Revenue

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
Regeneron's net profit in connection with commercialization of EYLEA outside the United States	$ 1,349.2	$ 1,107.9	$ 1,091.4
Reimbursement for manufacturing of commercial supplies[(1)]	60.1	78.2	54.2
Total Bayer collaboration revenue	$ 1,409.3	$ 1,186.1	$ 1,145.6

(1) Corresponding costs incurred by us in connection with such production is recorded within Cost of collaboration and contract manufacturing

Bayer records net product sales of EYLEA outside the United States. Regeneron's net profit in connection with commercialization of EYLEA outside the United States is summarized below:

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
EYLEA net product sales outside the United States	$ 3,592.4	$ 2,961.5	$ 2,897.4
Regeneron's share of collaboration profit from sales outside the United States	$ 1,408.3	$ 1,165.8	$ 1,148.0
Reimbursement of development expenses incurred by Bayer in accordance with Regeneron's payment obligation	(59.1)	(57.9)	(56.6)
Regeneron's net profit in connection with commercialization of EYLEA outside the United States	$ 1,349.2	$ 1,107.9	$ 1,091.4
Regeneron's net profit as a percentage of EYLEA net product sales outside the United States	38%	37%	38%

Roche Collaboration Revenue

As described in Part I, Item 1. "Business - Agreements Related to COVID-19 - Roche", Roche distributes and records net product sales of the casirivimab and imdevimab antibody cocktail outside the United States, and the parties share gross profits from worldwide sales, depending on the amount of manufactured product supplied by each party to the market. Each quarter, a single payment is due from one party to the other to true-up the global gross profits between the parties. If Regeneron is to receive a true-up payment from Roche, such amount will be recorded to Other collaboration revenue. If Regeneron is to make a true-up payment to Roche, such amount will be recorded to Cost of goods sold.

During the year ended December 31, 2021, the Company recorded $361.8 million of true-up payments, within Other collaboration revenue, from Roche in connection with this agreement.

Other Revenue

Other revenue decreased in 2021, compared to 2020, primarily due to lower amounts recognized in connection with our agreement with BARDA related to funding of certain development activities for COVID-19 antibodies, and, to a lesser extent, Inmazeb.

Expenses

	Year Ended December 31,			$ Change	
(In millions, except headcount data)	2021	2020	2019	2021 vs. 2020	2020 vs. 2019
Research and development[1]	$ 2,908.1	$ 2,735.0	$ 2,450.0	$ 173.1	$ 285.0
Selling, general, and administrative[1]	1,824.9	1,346.0	1,341.9	478.9	4.1
Cost of goods sold[2]	1,773.1	491.9	362.3	1,281.2	129.6
Cost of collaboration and contract manufacturing[3]	664.4	628.0	402.8	36.4	225.2
Other operating (income) expense, net	(45.6)	(280.4)	(209.2)	234.8	(71.2)
Total operating expenses	$ 7,124.9	$ 4,920.5	$ 4,347.8	$ 2,204.4	$ 572.7
Average headcount	9,884	8,495	7,773	1,389	722

[1] Includes costs incurred as well as cost reimbursements from collaborators who are not deemed to be our customers

[2] Cost of goods sold primarily includes costs in connection with producing commercial supplies for products that are sold by Regeneron in the United States (i.e., for which we record net product sales), any royalties we are obligated to pay on such sales, and amounts we are obligated to pay to collaborators for their share of gross profits.

[3] Cost of collaboration and contract manufacturing includes costs we incur in connection with producing commercial drug supplies for collaborators and others.

Operating expenses in 2021, 2020, and 2019 included a total of $601.7 million, $432.0 million, and $464.3 million, respectively, of non-cash compensation expense related to equity awards granted under our long-term incentive plans. As of December 31, 2021, unrecognized non-cash compensation expense related to unvested stock options and unvested restricted stock (including performance-based restricted stock units) was $515.9 million and $857.1 million, respectively. We expect to recognize this non-cash compensation expense related to stock options and restricted stock over weighted-average periods of 1.8 years and 3.0 years, respectively.

Research and Development Expenses

The following table summarizes our estimates of direct research and development expenses by clinical development program and other significant categories of research and development expenses. Direct research and development expenses are comprised primarily of costs paid to third parties for clinical and product development activities, including costs related to preclinical research activities, clinical trials, and the portion of research and development expenses incurred by our collaborators that we are obligated to reimburse. Indirect research and development expenses have not been allocated directly to each program, and primarily consist of costs to compensate personnel, overhead and infrastructure costs to maintain our facilities, and other costs related to activities that benefit multiple projects. Clinical manufacturing costs primarily consist of costs to manufacture bulk drug product for clinical development purposes as well as related external drug filling, packaging, and labeling costs. Clinical manufacturing costs also includes pre-launch commercial supplies which did not meet the criteria to be capitalized as inventory (see "Critical Accounting Policies and Use of Estimates - Inventories" above). The table below also includes reimbursements of research and development expenses by collaborators, as when we are entitled to reimbursement of all or a portion of such expenses that we incur under a collaboration, we record those reimbursable amounts in the period in which such costs are incurred.

	Year Ended December 31,			$ Change	
(In millions)	**2021**	**2020***	**2019***	**2021 vs. 2020**	**2020 vs. 2019**
Direct research and development expenses:					
REGEN-COV (casirivimab and imdevimab)	$ 309.8	$ 290.7	—	$ 19.1	$ 290.7
Dupixent (dupilumab)	146.4	129.7	$ 104.3	16.7	25.4
Libtayo (cemiplimab)	146.2	155.3	160.8	(9.1)	(5.5)
EYLEA and aflibercept 8 mg	102.2	72.2	55.4	30.0	16.8
Fasinumab	67.7	167.8	203.4	(100.1)	(35.6)
Up-front payments related to license and collaboration agreements	44.0	85.0	430.0	(41.0)	(345.0)
Other product candidates in clinical development and other research programs	427.9	494.5	355.7	(66.6)	138.8
Total direct research and development expenses	1,244.2	1,395.2	1,309.6	(151.0)	85.6
Indirect research and development expenses:					
Payroll and benefits	981.4	816.6	705.8	164.8	110.8
Lab supplies and other research and development costs	142.0	138.3	119.9	3.7	18.4
Occupancy and other operating costs	414.9	335.7	304.7	79.2	31.0
Total indirect research and development expenses	1,538.3	1,290.6	1,130.4	247.7	160.2
Clinical manufacturing costs	621.7	686.1	596.6	(64.4)	89.5
Reimbursement of research and development expenses by collaborators	(496.1)	(636.9)	(586.6)	140.8	(50.3)
Total research and development expenses	$ 2,908.1	$ 2,735.0	$ 2,450.0	$ 173.1	$ 285.0

* Certain prior year amounts have been reclassified to conform to the current year's presentation

Research and development expenses in 2021 included $34.0 million in aggregate up-front payments in connection with our collaboration agreement with Nykode Therapeutics, in 2020 included $85.0 million in aggregate up-front payments in connection with our collaboration agreement with Intellia, and in 2019 included a $400.0 million up-front payment to Alnylam. Research and development expenses included non-cash compensation expense of $316.6 million and $238.6 million in 2021 and 2020, respectively.

Reimbursement of research and development expenses by collaborators included reimbursements from Roche related to REGEN-COV of $128.1 million and $78.5 million for the years ended December 31, 2021 and 2020, respectively.

There are numerous uncertainties associated with drug development, including uncertainties related to safety and efficacy data from each phase of drug development, uncertainties related to the enrollment and performance of clinical trials, changes in

regulatory requirements, changes in the competitive landscape affecting a product candidate, and other risks and uncertainties described in Part I, Item 1A. "Risk Factors" (including those relating to the disruptions caused by the COVID-19 pandemic). There is also variability in the duration and costs necessary to develop a pharmaceutical product, potential opportunities and/or uncertainties related to future indications to be studied, and the estimated cost and scope of the projects. The lengthy process of seeking FDA and other applicable approvals, and subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources. Any failure by us to obtain, or delay in obtaining, regulatory approvals could materially adversely affect our business. We are unable to reasonably estimate if our product candidates in clinical development will generate material product revenues and net cash inflows.

Selling, General, and Administrative Expenses

Selling, general, and administrative expenses increased in 2021, compared to 2020, primarily due to an increase in commercialization-related expenses for (i) EYLEA, including direct-to-consumer advertising, (ii) REGEN-COV, including costs associated with educational campaigns related to COVID-19, and (iii) Libtayo; and higher headcount-related costs. In addition, in 2020, we recorded a reversal of accruals for litigation-related loss contingencies as a result of the October 2020 ruling by the Technical Board of Appeal of the EPO and its impact on certain patent infringement actions in Europe relating to Praluent (see Note 15 to our Consolidated Financial Statements for additional details). Selling, general, and administrative expenses also included $213.3 million and $153.0 million of non-cash compensation expense in 2021 and 2020, respectively.

Cost of Goods Sold

Cost of goods sold increased in 2021, compared to 2020, primarily due to the recognition of manufacturing costs in connection with the product sales of REGEN-COV. During 2021, the Company also recorded a $259.6 million true-up payment owed in connection with global gross profits under our Roche collaboration agreement described above. Additionally, during the fourth quarter of 2021, the Company recorded a $231.7 million charge to write down its REGEN-COV inventory as a result of data that showed REGEN-COV was highly unlikely to be active against the Omicron variant and the FDA revision of the EUA for REGEN-COV, pursuant to which REGEN-COV was no longer authorized for use in any U.S. states, territories, or jurisdictions. Refer to Part I, Item 1. "Business - Products - REGEN-COV - Emergency and Temporary Use Authorizations" for additional information.

Cost of Collaboration and Contract Manufacturing

Cost of collaboration and contract manufacturing increased in 2021, compared to 2020, primarily due to the recognition of manufacturing costs associated with higher sales of Dupixent, partly offset by lower costs in connection with manufacturing ex-U.S. commercial supplies of Praluent for Sanofi and the recognition of process validation costs during 2020 in connection with manufacturing Inmazeb under our BARDA agreement as such costs did not recur during 2021.

Other Operating (Income) Expense

Other operating (income) expense, net, includes recognition of a portion of amounts previously deferred in connection with up-front and development milestone payments, as applicable, received in connection with Sanofi IO, Teva, and MTPC collaborative arrangements. In these arrangements, we satisfy our obligation(s) during the development phase over time, and, as a result, recognize amounts initially deferred over time using an input method on the basis of our research and development costs incurred relative to the total expected cost which determines the extent of our progress toward completion. See the Critical Accounting Policies and Use of Estimates section above for further details.

During 2021, we updated our estimate of the total research and development costs expected to be incurred (which resulted in a change to the estimate of the stage of completion) in connection with the Sanofi IO Collaboration, and, as a result, recorded a cumulative catch-up adjustment of $66.9 million as a reduction to other operating income. During 2020, we updated our estimate of the total research and development costs expected to be incurred (which resulted in changes to the estimate of the stage of completion) in connection with the Sanofi IO, Teva, and MTPC collaboration agreements, and therefore recorded cumulative catch-up adjustments of $99.8 million, net, as an increase to other operating income.

Other Income (Expense)

Other income (expense), net, was $379.0 million in 2021, compared to $233.8 million in 2020. This change was primarily driven by an increase in unrealized gains on equity securities of $190.1 million.

Income Taxes

(In millions, except effective tax rate)	Year Ended December 31, 2021	2020	2019
Income tax expense	$ 1,250.5	$ 297.2	$ 313.3
Effective tax rate	13.4%	7.8%	12.9%

Our effective tax rate for 2021 was positively impacted, compared to the U.S. federal statutory rate, primarily by income earned in foreign jurisdictions with tax rates lower than the U.S. federal statutory rate and stock-based compensation. Our effective tax rate for 2020 was positively impacted, compared to the U.S. federal statutory rate, primarily by stock-based compensation, and, to a lesser extent, federal tax credits for research activities and income earned in foreign jurisdictions with tax rates lower than the U.S. federal statutory rate.

Liquidity and Capital Resources

Our financial condition is summarized as follows:

(In millions)	As of December 31, 2021	2020	$ Change
Financial assets:			
Cash and cash equivalents	$ 2,885.6	$ 2,193.7	$ 691.9
Marketable securities - current	2,809.1	1,393.3	1,415.8
Marketable securities - noncurrent	6,838.0	3,135.6	3,702.4
	$ 12,532.7	$ 6,722.6	$ 5,810.1
Borrowings:			
Long-term debt	$ 1,980.0	$ 1,978.5	$ 1.5
Working capital:			
Current assets	$ 14,014.9	$ 9,779.1	$ 4,235.8
Current liabilities	3,932.5	2,697.4	1,235.1
	$ 10,082.4	$ 7,081.7	$ 3,000.7

As of December 31, 2021, we also had borrowing availability of $750.0 million under a revolving credit facility (see further description under "*Credit Facility*" below).

Sources and Uses of Cash for the Years Ended December 31, 2021, 2020, and 2019

(In millions)	As of December 31, 2021	2020	2019	$ Change 2021 vs. 2020	2020 vs. 2019
Cash flows provided by operating activities	$ 7,081.3	$ 2,618.1	$ 2,430.0	$ 4,463.2	$ 188.1
Cash flows used in investing activities	$ (5,384.7)	$ (70.6)	$ (2,027.8)	$ (5,314.1)	$ 1,957.2
Cash flows used in financing activities	$ (1,005.8)	$ (1,970.5)	$ (252.1)	$ 964.7	$ (1,718.4)

Cash Flows from Operating Activities

2021

As of December 31, 2021, Accounts receivable had increased by $1.927 billion, compared to December 31, 2020, primarily due to REGEN-COV sales in connection with our September 2021 agreement to supply drug product to the U.S. government. Other non-cash items, net, in 2021 included inventory write-offs and reserves totaling $457.1 million, primarily related to REGEN-COV. Accounts payable, accrued expenses, and other liabilities as of December 31, 2021 included a $259.6 million fourth quarter 2021 true-up payment owed in connection with global gross profits under our Roche collaboration agreement.

2020

As of December 31, 2020, Accounts receivable had increased by $1.356 billion, compared to December 31, 2019, partly as a result of extending payment terms to EYLEA customers due to the COVID-19 pandemic. Inventories increased as of December 31, 2020, compared to December 31, 2019, partially as a result of purchasing additional raw materials in anticipation of potential disruptions to our supply chain due to the COVID-19 pandemic.

2019

Deferred taxes as of December 31, 2019 increased by $130.6 million, compared to December 31, 2018, primarily due to the tax treatment of the up-front payment made to Alnylam and non-cash compensation expense. Accounts payable, accrued expenses, and other liabilities as of December 31, 2019 increased compared to December 31, 2018 partially due to the impact of the receipt of a $461.9 million payment from Sanofi in connection with the termination of the 2015 IO Discovery Agreement.

Cash Flows from Investing Activities

Sales of marketable securities in 2020 included proceeds in connection with funding our stock repurchase from Sanofi (as described below). In 2019, we purchased $400.0 million of Alnylam common stock in connection with entering into the collaboration agreement. Capital expenditures in 2021 included costs associated with the expansion of our manufacturing facilities in Rensselaer, New York (including the ongoing construction of a fill/finish facility and related equipment) and Limerick, Ireland, as well as initial costs incurred in connection with our planned expansion of the Tarrytown, New York campus. We expect to incur capital expenditures of $650 million to $730 million in 2022 primarily in connection with the continued expansion of our manufacturing facilities (including the fill/finish facility) and the expansion of our research, preclinical manufacturing, and support facilities at our Tarrytown, New York campus. We also expect continued significant capital expenditures over the next several years in connection with the planned expansion of our Tarrytown, New York campus.

Cash Flows from Financing Activities

Proceeds from issuances of Common Stock, in connection with exercises of employee stock options, were $1.672 billion during 2021, compared to $2.575 billion during 2020 and $211.8 million during 2019. For additional information related to cash flows from financing activities, see "Share Repurchase Program", "Sanofi Funding of Certain Development Costs", "Secondary Offering and Purchase of Regeneron Common Stock Held by Sanofi", and "Issuance of Senior Notes" sections below.

Credit Facility

In December 2018, we entered into an agreement with a syndicate of lenders (the "Credit Agreement") which provides for a $750.0 million senior unsecured five-year revolving credit facility (the "Credit Facility"). The Credit Agreement includes an option for us to elect to increase the commitments under the Credit Facility and/or to enter into one or more tranches of term loans in the aggregate principal amount of up to $250.0 million, subject to the consent of the lenders providing the additional commitments or term loans, as applicable, and certain other conditions. Proceeds of the loans under the Credit Facility may be used to finance working capital needs, and for general corporate or other lawful purposes, of Regeneron and its subsidiaries. The Credit Agreement also provides a $50.0 million sublimit for letters of credit. The Credit Agreement includes an option for us to elect to extend the maturity date of the Credit Facility beyond December 2023, subject to the consent of the extending lenders and certain other conditions. Amounts borrowed under the Credit Facility may be prepaid, and the commitments under the Credit Facility may be terminated, at any time without premium or penalty. We had no borrowings outstanding under the Credit Facility as of December 31, 2021.

The Credit Agreement contains financial and operating covenants. Financial covenants include a maximum total leverage ratio and a minimum interest expense coverage ratio. We were in compliance with all covenants of the Credit Facility as of December 31, 2021.

Share Repurchase Programs

In November 2019, our board of directors authorized a share repurchase program to repurchase up to $1.0 billion of our Common Stock. The share repurchase program permitted the Company to make repurchases through a variety of methods, including open-market transactions (including pursuant to a trading plan adopted in accordance with Rule 10b5-1 of the Exchange Act), privately negotiated transactions, accelerated share repurchases, block trades, and other transactions in compliance with Rule 10b-18 of the Exchange Act. As of December 31, 2020, the Company had repurchased the entire $1.0 billion of its Common Stock that it was authorized to repurchase under the program.

In January 2021, our board of directors authorized a share repurchase program to repurchase up to $1.5 billion of our Common Stock. The share repurchase program was approved under terms substantially similar to the November 2019 share repurchase program. As of December 31, 2021, the Company had repurchased the entire $1.5 billion of its Common Stock that it was authorized to repurchase under the program.

In November 2021, our board of directors authorized an additional share repurchase program to repurchase up to $3.0 billion of our Common Stock. The share repurchase program was approved under terms substantially similar to the share repurchase programs above. Repurchases may be made from time to time at management's discretion, and the timing and amount of any such repurchases will be determined based on share price, market conditions, legal requirements, and other relevant factors. The program has no time limit and can be discontinued at any time. There can be no assurance as to the timing or number of shares of any repurchases in the future. We plan to finance the share repurchase program with available cash. As of December 31, 2021, $2.845 billion remained available for share repurchases under the November 2021 program.

The table below summarizes the shares of our Common Stock we repurchased under the programs described above and the cost of the shares received, which were recorded as Treasury Stock.

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
Number of shares repurchased	3.0	1.6	0.7
Total cost of shares received	$ 1,655.0	$ 746.0	$ 254.0

Sanofi Funding of Certain Development Costs

Pursuant to a 2018 agreement, we agreed to allow Sanofi to satisfy in whole or in part its funding obligations with respect to Libtayo development and/or certain activities relating to dupilumab and itepekimab incurred in periods through September 30, 2020 by selling shares of our Common Stock owned by Sanofi. During 2020, Sanofi elected to sell, and we elected to purchase, shares of our Common Stock to satisfy Sanofi's funding obligation related to such activities. Consequently, we recorded the cost of the shares received, or $135.0 million, as Treasury Stock during 2020. In addition, during 2019, Sanofi elected to sell, and we elected to purchase, shares of our Common Stock to satisfy Sanofi's funding obligation. Consequently, we recorded the cost of the shares received, or $102.7 million, as Treasury Stock during 2019.

Secondary Offering and Purchase of Regeneron Common Stock Held by Sanofi

In May 2020, a secondary offering of 13,014,646 shares of our Common Stock (the "Secondary Offering") held by Sanofi was completed. In connection with the Secondary Offering, we also purchased 9,806,805 shares of our Common Stock directly from Sanofi for an aggregate purchase amount of $5.0 billion (the "Stock Purchase").

We funded the Stock Purchase with a combination of cash on hand, proceeds from the sale of marketable securities, and proceeds from loans under a $1.5 billion senior unsecured bridge loan facility (the "Bridge Facility") which was entered into in May 2020. The Bridge Facility was repaid in August 2020 following the issuance and sale of the Company's senior unsecured notes.

Issuance of Senior Notes

In August 2020, we issued and sold $1.250 billion aggregate principal amount of senior unsecured notes due 2030 (the "2030 Notes") and $750 million aggregate principal amount of senior unsecured notes due 2050 (the "2050 Notes" and, together with the 2030 Notes, the "Notes"). Net proceeds from the issuance and sale of the Notes (after deducting underwriting discounts and offering expenses) were used in part to repay in full the Bridge Facility described above, including accrued interest and related fees and expenses in connection therewith.

The 2030 Notes accrue interest at the rate of 1.750% per year and will mature on September 15, 2030. The 2050 Notes accrue interest at the rate of 2.800% per year and will mature on September 15, 2050. Interest on each series of Notes is payable semi-annually in arrears on March 15 and September 15 of each year until their respective maturity dates.

The Notes may be redeemed at the Company's option at any time at 100% of the principal amount plus accrued and unpaid interest, and, until a specified period before maturity, a specified make-whole amount. The Notes contain a change-of-control provision that, under certain circumstances, may require the Company to offer to repurchase the Notes at a price equal to 101% of the principal amount plus accrued and unpaid interest.

The Notes also contain certain limitations on the Company's ability to incur liens and enter into sale and leaseback transactions, as well as customary events of default.

Tarrytown, New York Leases

We lease laboratory and office facilities in Tarrytown, New York (the "Facility"). In 2016, we entered into a Purchase Agreement with the then lessor, pursuant to which we agreed to purchase the Facility for a purchase price of $720.0 million. In March 2017, we entered into a Participation Agreement with BA Leasing BSC, LCC, and affiliate of Banc of America Leasing & Capital, LLC ("BAL"), as lessor, and a syndicate of lenders (collectively with BAL, the "Lease Participants"), which provided for lease financing in connection with the acquisition by BAL of the Facility and our lease of the Facility from BAL. In March 2017, we assigned our right to take title to the Facility under the Purchase Agreement to BAL, and the Lease Participants advanced $720.0 million, which was used by BAL to finance the purchase price for the Facility.

Concurrent with entering into the Participation Agreement, we also entered into a lease agreement (the "Lease") for the Facility with BAL for a five-year term ending in March 2022. The Lease requires us to pay all maintenance, insurance, taxes, and other costs arising out of the use of the Facility. We are also required to make monthly payments of basic rent during the term of the Lease in an amount equal to a variable rate per annum based on the one-month LIBOR, plus an applicable margin that varies with our debt rating and total leverage ratio.

The Participation Agreement and the Lease include an option for us to elect to extend the maturity date of the Participation Agreement and the term of the Lease for an additional five-year period, subject to the consent of all the Lease Participants and certain other conditions. We also have the option prior to the end of the term of the Lease to (a) purchase the Facility by paying an amount equal to the outstanding principal amount of the Lease Participants' advances under the Participation Agreement, all accrued and unpaid interest and yield thereon, and all other outstanding amounts under the Participation Agreement, the Lease, and certain related documents or (b) sell the Facility to a third party on behalf of BAL. The advances under the Participation Agreement mature, and all amounts outstanding thereunder will become due and payable in full at the end of the term of the Lease.

In September 2021, we delivered a request to the Lease Participants to potentially exercise the option for a five-year extension of the term of the Lease and the maturity date under the Participation Agreement. In November 2021, the Lease Participants consented to such extension, subject to the satisfaction of certain conditions prior to the expiration of the existing term in March 2022, including the negotiation and execution of satisfactory definitive documentation setting forth the terms and conditions that would apply during such potential extended term. We are negotiating such documentation with the Lease Participants, but there can be no assurance that such extension will become effective.

The agreements governing the Lease financing contain financial and operating covenants. Such financial covenants and certain of the operating covenants are substantially similar to the covenants set forth in our Credit Facility. We were in compliance with all such covenants as of December 31, 2021.

Additional Funding Requirements

The amount required to fund operations will depend on various factors, including the potential regulatory approval and commercialization of our product candidates and the timing thereof and the extent and cost of our research and development programs. We believe that our existing capital resources, borrowing availability under the Credit Facility, funds generated by anticipated product sales, and, as described above under Part I, Item 1. "Business - Collaboration, License, and Other Agreements," funding for reimbursement of research and development costs that we are entitled to receive under our collaboration agreements, will enable us to meet our anticipated operating needs for the foreseeable future.

We expect continued increases in our expenditures, particularly in connection with our research and development activities (including preclinical and clinical programs). The amount of funding that will be required for our clinical programs depends upon the results of our research and preclinical programs and early-stage clinical trials, regulatory requirements, the duration and results of clinical trials underway and of additional clinical trials that we decide to initiate, and the various factors that affect the cost of each trial, including the size of trials, fees charged for services provided by clinical trial investigators and other third parties, the costs for manufacturing the product candidate for use in the trials, and other expenses. Under certain collaboration agreements, the amount of funding for reimbursement of research and development costs that we are entitled to receive is capped at a specified amount; therefore, we may elect to independently fund certain research and development costs in excess of such capped amounts.

We expect to continue to incur development and manufacturing costs for our COVID-19 monoclonal antibodies in 2022, though the amount of funding that will be required will be subject to clinical data results, quantity of drug supply manufactured, the duration of the COVID-19 pandemic, and other factors, including regulatory outcomes, as described in Part I.

We anticipate continuing to incur substantial commercialization costs for EYLEA, Dupixent, and Libtayo. Commercialization costs over the next few years will depend on, among other things, the market potential for product candidates, whether commercialization costs are shared with a collaborator, and regulatory approval of additional product candidates.

We expect that expenses related to the filing, prosecution, defense, and enforcement of patents and other intellectual property will be substantial.

Liabilities for unrecognized tax benefits totaled $410.9 million at December 31, 2021. Due to their nature, there is a high degree of uncertainty regarding the period and amounts of potential future cash settlement with tax authorities. See Note 14 to our Consolidated Financial Statements. In addition, the Tax Cuts and Jobs Act of 2017 requires the capitalization and amortization of research and development expenses effective for years beginning after December 31, 2021, which we expect will have a material impact on our cash flows beginning in 2022.

We enter into collaboration and licensing agreements that may require us to pay (i) amounts contingent upon the occurrence of various future events (e.g., upon the achievement of various development and commercial milestones), which, in the aggregate, could be significant, and/or (ii) royalties calculated based on a percentage of net product sales. The payment of these amounts, however, is contingent upon the occurrence of various future events, which have a high degree of uncertainty of occurring and for which the specific timing cannot be predicted. See Note 3 and Note 10 to our Consolidated Financial Statements.

Under our collaboration with Bayer for EYLEA outside the United States and our Antibody and IO Collaborations with Sanofi, we and our collaborator share profits and losses in connection with commercialization of drug products. If the applicable collaboration is profitable, we have contingent contractual obligations to reimburse Bayer and Sanofi for a defined percentage (generally 50%) of agreed-upon development expenses funded by Bayer and Sanofi (i.e., "development balance"). These reimbursements are deducted each quarter, in accordance with a formula, from our share of the collaboration profits (and, for our EYLEA collaboration with Bayer, inclusive of our percentage on product sales in Japan) otherwise payable to us, unless, in the case of EYLEA, we elect to reimburse these expenses at a faster rate. As of December 31, 2021, our contingent reimbursement obligation to Bayer for EYLEA was approximately $282 million and our contingent reimbursement obligation to Sanofi in connection with the companies' Antibody Collaboration and IO Collaboration was approximately $3.152 billion and $103 million, respectively. Therefore, we expect that, for the foreseeable future, a portion of our share of profits from sales under our collaborations with Bayer and Sanofi will be used to reimburse our collaborators for these obligations.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that are currently material or reasonably likely to be material to our consolidated financial position or results of operations.

Future Impact of Recently Issued Accounting Standards

As of December 31, 2021, the future adoption of recently issued accounting standards is not expected to have a material impact on the Company's financial position or results of operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Our earnings and cash flows are subject to fluctuations due to changes in interest rates, principally in connection with our investments in marketable securities, which consist primarily of corporate bonds. We do not believe we are materially exposed to changes in interest rates related to our investments, and we do not currently use interest rate derivative instruments to manage exposure to interest rate changes of our investments. We estimate that a 100 basis point, or 1%, unfavorable change in interest rates would have resulted in approximately a $120.0 million and $48.1 million decrease in the fair value of our investment portfolio as of December 31, 2021 and 2020, respectively.

We have exposure to market risk for changes in interest rates, including the interest rate risk relating to our variable rate Tarrytown, New York lease (as described in Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources - *Tarrytown, New York Leases*"). Our interest rate exposure is primarily offset by our investments in marketable securities. In addition, we further manage our interest rate exposure related to our variable rate lease through the use of derivative instruments. All of our derivative instruments are utilized for risk management purposes and are not used for trading or speculative purposes. We continue to monitor our interest rate risk and may utilize additional derivative instruments and/or other strategies in the future to further mitigate our interest rate exposure.

We have hedged a portion of our floating interest rate exposure using interest rate swap and interest rate cap contracts. We estimate that a 100 basis point, or 1%, unfavorable change in interest rates would not have a material impact on the fair value of our interest rate swap or interest rate cap contracts.

Credit Quality Risk

We have an investment policy that includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and concentration and diversification. Nonetheless, deterioration of the credit quality of an investment security subsequent to purchase may subject us to the risk of not being able to recover the full principal value of the security. In 2021, 2020, and 2019, we did not record any charges for credit-related impairments of our available-for-sale debt securities.

We are subject to credit risk associated with the receivables due from our collaborators, including Bayer and Sanofi. We are also subject to credit risk in connection with trade accounts receivable due from our customers from our product sales. We have contractual payment terms with each of our collaborators and customers, and we monitor their financial performance and credit worthiness so that we can properly assess and respond to any changes in their credit profile. In 2021, 2020 and 2019, we did not recognize any charges for write-offs and allowances of accounts receivable related to credit risk for our collaborators or customers. As of December 31, 2021, three customers accounted on a combined basis for 91% (including 29% related to the U.S. government) of our net trade accounts receivables.

Foreign Exchange Risk

As discussed further above, our collaborators market certain products outside the United States, and we share in profits and losses with these collaborators from commercialization of products. In addition, pursuant to the applicable terms of the agreements with our collaborators, we also share in certain worldwide development expenses incurred by our collaborators. We also incur worldwide development expenses for clinical products we are developing independently, in addition to incurring expenses outside of the United States in connection with our international operations. Therefore, significant changes in foreign exchange rates of the countries outside the United States where our products are sold, where development expenses are incurred by us or our collaborators, or where we incur operating expenses can impact our operating results and financial condition. As sales outside the United States continue to grow, and as we expand our international operations, we will continue to assess potential steps, including foreign currency hedging and other strategies, to mitigate our foreign exchange risk.

Market Price Risk

We are exposed to price risk on equity securities included in our investment portfolio. Our marketable securities include equity investments in publicly traded stock of companies, including common stock of companies with which we have entered into collaboration arrangements. Changes in the fair value of our equity investments are included in Other income (expense), net on the Consolidated Statements of Income. We recorded $386.1 million and $196.0 million of net unrealized gains on equity securities in Other income (expense), net for the years ended December 31, 2021 and 2020, respectively.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item is included on pages F-1 through F-42 of this report and is incorporated herein by reference.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")), as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our principal executive officer and principal financial officer each concluded that, as of the end of such period, our disclosure controls and procedures were effective in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported on a timely basis, and is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosures.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2021 using the framework in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management has concluded that our internal control over financial reporting was effective as of December 31, 2021. The effectiveness of the Company's internal control over financial reporting as of December 31, 2021 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears under Part IV, Item 15.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Our management, including our principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures or internal controls over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the system are met and cannot detect all deviations. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud or deviations, if any, within the company have been detected. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item (other than the information set forth in the next paragraph in this Item 10) will be included in our definitive proxy statement with respect to our 2022 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to our officers, directors, and employees. The full text of our code of business conduct and ethics can be found on our website (http://www.regeneron.com) under the "Corporate Governance" heading on the "Investors & Media" page. We may satisfy the disclosure requirements under Item 5.05 of Form 8-K regarding an amendment to, or a waiver from, a provision of our code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, or controller, or persons performing similar functions, by posting such information on our website where it is accessible through the same link noted above.

ITEM 11. EXECUTIVE COMPENSATION

The information called for by this item will be included in our definitive proxy statement with respect to our 2022 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information called for by this item will be included in our definitive proxy statement with respect to our 2022 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information called for by this item will be included in our definitive proxy statement with respect to our 2022 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information called for by this item will be included in our definitive proxy statement with respect to our 2022 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) *1. Financial Statements*

The consolidated financial statements filed as part of this report are listed on the Index to Financial Statements on page F-1.

2. Financial Statement Schedules

All schedules for which provision is made in the applicable accounting regulations of the Securities and Exchange Commission are not required under the related instructions or are inapplicable and, therefore, have been omitted.

3. Exhibits

Exhibit Number	Description
3.1	Restated Certificate of Incorporation, as amended. (Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. (the "Registrant"), for the quarter ended June 30, 2015, filed August 4, 2015.)
3.2	Amended and Restated By-Laws. (Incorporated by reference from the Form 8-K for the Registrant filed December 21, 2016.)
4.1	Description of Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
4.2	Indenture, dated August 12, 2020, between the Registrant and U.S. Bank National Association. (Incorporated by reference from the Form 8-K for the Registrant, filed August 12, 2020.)
4.3	First Supplemental Indenture, dated August 12, 2020, between the Registrant and U.S. Bank National Association. (Incorporated by reference from the Form 8-K for the Registrant, filed August 12, 2020.)
4.4	Form of 1.750% Senior Note due 2030 (included in Exhibit 4.3).
4.5	Form of 2.800% Senior Note due 2050 (included in Exhibit 4.3).
10.1 +	Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan. (Incorporated by reference from the Registration Statement on Form S-8 for the Registrant, filed June 13, 2011.)
10.1.1 +	Form of option agreement and related notice of grant for use in connection with the grant of time based vesting stock options to the Registrant's non-employee directors and executive officers under the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2009, filed April 30, 2009.)
10.1.2 +	Form of option agreement and related notice of grant for use in connection with the grant of performance based vesting stock options to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2009, filed April 30, 2009.)
10.1.3 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2010, filed February 17, 2011.)
10.1.4 +	Form of option agreement and related notice of grant for use in connection with the grant of performance based vesting stock options to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2010, filed February 17, 2011.)
10.1.5 +	Form of option agreement and related notice of grant for use in connection with the grant of time based vesting stock options to the Registrant's non-employee directors under the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2011, filed February 21, 2012.)

10.1.6 +	Amendment No. 1 to the Regeneron Pharmaceuticals, Inc. Second Amended and Restated 2000 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2013, filed February 13, 2014.)
10.2 +	Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Registration Statement on Form S-8 for the Registrant, filed June 12, 2017.)
10.2.1 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 8-K for the Registrant, filed June 18, 2014.)
10.2.2 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 8-K for the Registrant, filed June 18, 2014.)
10.2.3 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 8-K for the Registrant, filed June 18, 2014.)
10.2.4 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to P. Roy Vagelos, M.D. under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2015, filed February 11, 2016.)
10.2.5 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 8-K for the Registrant, filed November 19, 2015.)
10.2.6 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 8-K for the Registrant, filed November 19, 2015.)
10.2.7 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2015, filed February 11, 2016.)
10.2.8 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2017, filed February 8, 2018.)
10.2.9 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to P. Roy Vagelos, M.D. under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2017, filed February 8, 2018.)
10.2.10 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2017, filed February 8, 2018.)
10.2.11 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2017, filed February 8, 2018.)
10.2.12 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2018). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019.)

10.2.13 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to P. Roy Vagelos, M.D. under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2018). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019.)
10.2.14 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2018). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019.)
10.2.15 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2018). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019.)
10.2.16 +	Form of restricted stock unit award agreement and related notice of grant for use in connection with the grant of restricted stock units to the Registrant's non-employee directors under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019.)
10.2.17 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2019). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.2.18 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to P. Roy Vagelos, M.D. under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2019). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.2.19 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2019). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.2.20 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2019). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.2.21 +	Form of restricted stock unit award agreement and related notice of grant for use in connection with the grant of restricted stock units to the Registrant's non-employee directors under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (revised 2019). (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.2.22 +	Form of performance restricted stock unit award agreement and related notice of grant for use in connection with the grant of performance restricted stock units to Leonard S. Schleifer, M.D., Ph.D., George D. Yancopoulos, M.D., Ph.D., and P. Roy Vagelos, M.D. under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.3 +	Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Registration Statement on Form S-8 for the Registrant, filed June 16, 2020.)
10.3.1 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's executive officers under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.3.2 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to P. Roy Vagelos, M.D. under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)

10.3.3 +	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.3.4 +	Form of restricted stock unit award agreement and related notice of grant for use in connection with the grant of restricted stock units to P. Roy Vagelos, M.D. under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.3.5 +	Form of stock option agreement and related notice of grant for use in connection with the grant of non-qualified stock options to the Registrant's non-employee directors under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.3.6 +	Form of restricted stock unit award agreement and related notice of grant for use in connection with the grant of restricted stock units to the Registrant's non-employee directors under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.3.7 +	Form of performance restricted stock unit award agreement and related notice of grant for use in connection with the grant of performance restricted stock units to Leonard S. Schleifer, M.D., Ph.D. and George D. Yancopoulos, M.D., Ph.D. under the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.4 +	Amended and Restated Employment Agreement, dated as of November 14, 2008, between the Registrant and Leonard S. Schleifer, M.D., Ph.D. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2008, filed February 26, 2009.)
10.5* +	Employment Agreement, dated as of December 31, 1998, between the Registrant and P. Roy Vagelos, M.D. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2004, filed March 11, 2005.)
10.6 +	Offer Letter for Robert E. Landry effective September 9, 2013. (Incorporated by reference from the Form 8-K for the Registrant, filed September 12, 2013.)
10.7 +	Regeneron Pharmaceuticals, Inc. Change in Control Severance Plan, amended and restated effective as of November 14, 2008. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2008, filed February 26, 2009.)
10.8 +	Regeneron Pharmaceuticals, Inc. Cash Incentive Bonus Plan. (Incorporated by reference from the Form 8-K for the Registrant, filed June 17, 2015.)
10.9*	IL-1 Antibody Termination Agreement by and between Novartis Pharma AG, Novartis Pharmaceuticals Corporation and the Registrant, dated as of June 8, 2009. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2009, filed August 4, 2009.)
10.10*	Amended and Restated Collaboration Agreement, dated as of February 23, 2015, by and between Sanofi-Aventis US LLC and the Registrant. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2015, filed May 7, 2015.)
10.11*	License and Collaboration Agreement, dated as of October 18, 2006, by and between Bayer HealthCare LLC and the Registrant. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2006, filed November 6, 2006.)
10.11.1*	Restated Amendment Agreement, dated December 30, 2014 and entered into effective as of May 7, 2012, by and between Bayer HealthCare LLC and the Registrant. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2014, filed February 12, 2015.)
10.11.2**	Second Amendment Agreement, dated December 19, 2019, by and between Bayer HealthCare LLC and the Registrant. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2019, filed February 7, 2020.)
10.12	License and Collaboration Agreement, dated as of January 10, 2014, by and between Bayer HealthCare LLC and the Registrant. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2014, filed May 8, 2014.)

10.13*	Amended and Restated Discovery and Preclinical Development Agreement, dated as of November 10, 2009, by and between Aventis Pharmaceuticals Inc. and the Registrant. (Incorporated by reference from the Form 10-K/A for the Registrant, for the year ended December 31, 2009, filed June 2, 2010.)
10.13.1*	Amendment No. 1 to Amended and Restated Discovery and Preclinical Development Agreement, dated July 27, 2015 and entered into effective as of July 1, 2015, by and between the Registrant and Sanofi Biotechnology SAS, as successor-in-interest to Aventis Pharmaceuticals, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2015, filed November 4, 2015.)
10.14*	Amended and Restated License and Collaboration Agreement, dated as of November 10, 2009, by and among Aventis Pharmaceuticals Inc., sanofi-aventis Amerique du Nord, and the Registrant. (Incorporated by reference from the Form 10-K/A for the Registrant, for the year ended December 31, 2009, filed June 2, 2010.)
10.14.1*	First Amendment to Amended and Restated License and Collaboration Agreement by and between the Registrant and Aventis Pharmaceuticals Inc., dated May 1, 2013. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2013, filed August 6, 2013.)
10.14.2*	Amendment No. 2 to Amended and Restated License and Collaboration Agreement, dated July 27, 2015 and entered into effective as of July 1, 2015, by and between the Registrant and Sanofi Biotechnology SAS, as successor-in-interest to Aventis Pharmaceuticals, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2015, filed November 4, 2015.)
10.14.3**	Third Amendment to Amended and Restated License and Collaboration Agreement, dated as of April 5, 2020, and effective as of April 1, 2020, by and between the Registrant, Sanofi Biotechnology SAS, and Sanofi. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2020, filed August 5, 2020.)
10.14.4**	Fourth Amendment to Amended and Restated License and Collaboration Agreement, dated as of October 6, 2021, by and between the Registrant, Sanofi Biotechnology SAS, and Sanofi.
10.15**	Praluent Cross License & Commercialization Agreement, dated as of April 5, 2020, and effective as of April 1, 2020, by and between the Registrant and Sanofi Biotechnology SAS. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2020, filed August 5, 2020.)
10.16	Amended and Restated Investor Agreement, dated as of January 11, 2014, by and among Sanofi, sanofi-aventis US LLC, Aventis Pharmaceuticals Inc., sanofi-aventis Amerique du Nord, and the Registrant. (Incorporated by reference from the Form 8-K for the Registrant, filed January 13, 2014.)
10.16.1	Amendment to the Amended and Restated Investor Agreement, dated as of May 25, 2020, by and among the Registrant, Sanofi, Sanofi-Aventis US LLC, and Aventisub LLC. (Incorporated by reference from the Form 8-K for the Registrant, filed May 29, 2020.)
10.17*	Letter Agreement by and between the Registrant and Aventis Pharmaceuticals Inc., dated May 2, 2013. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2013, filed August 6, 2013.)
10.18	Credit Agreement, dated as of December 14, 2018, by and among the Registrant, as a borrower and guarantor; certain direct subsidiaries of the Registrant, as the initial subsidiary borrowers; JPMorgan Chase Bank, N.A., as administrative agent; Bank of America, N.A. and U.S. Bank National Association, as co-syndication agents; Barclays Bank PLC, Citibank, N.A., Fifth Third Bank, and MUFG Bank, Ltd., as co-documentation agents; JPMorgan Chase Bank, N.A., Bank of America, N.A., and U.S. Bank National Association, as the issuing banks; JPMorgan Chase Bank, N.A., as the swingline lender; and the other lenders party thereto from time to time. (Incorporated by reference from the Form 8-K for the Registrant, filed December 17, 2018.)
10.18.1	Amendment No. 1 to Credit Agreement, dated as of November 11, 2021, by and among the Registrant, as a borrower and guarantor; certain direct subsidiaries of the Registrant, as subsidiary borrowers; JPMorgan Chase Bank, N.A., as administrative agent; and the lenders party thereto.
10.19*	Amended and Restated Immuno-oncology Discovery and Development Agreement, executed on January 2, 2019 and effective as of December 31, 2018, by and between the Registrant and Sanofi Biotechnology SAS. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2018, filed February 7, 2019).
10.20*	Immuno-oncology License and Collaboration Agreement, dated July 27, 2015 and entered into effective as of July 1, 2015, by and between the Registrant and Sanofi Biotechnology SAS. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2015, filed November 4, 2015.)

10.20.1**	First Amendment to Immuno-oncology License and Collaboration Agreement, dated as of October 6, 2021, by and between the Registrant and Sanofi Biotechnology SAS.
10.21*	Collaboration Agreement, dated as of September 29, 2015, by and between Regeneron Ireland and Mitsubishi Tanabe Pharma Corporation. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2015, filed November 4, 2015.)
10.22*	ANG2 License and Collaboration Agreement, dated as of March 23, 2016, by and between Bayer HealthCare LLC and the Registrant. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2016, filed May 5, 2016.)
10.23*	Collaboration Agreement, dated as of September 17, 2016, by and between Teva Pharmaceuticals International GmbH and Regeneron Ireland. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2016, filed November 4, 2016.)
10.24*	Purchase Agreement, dated as of December 30, 2016, by and among BMR-Landmark at Eastview LLC and BMR-Landmark at Eastview IV LLC and the Registrant. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2016, filed February 9, 2017.)
10.25	Amended and Restated Participation Agreement, dated as of May 2, 2019, by and among Old Saw Mill Holdings LLC, as lessee; Bank of America, N.A., as administrative agent; BA Leasing BSC, LLC, as lessor; and the lenders party thereto from time to time. (Incorporated by reference from the Form 8-K for the Registrant, filed May 3, 2019.)
10.25.1	First Amendment to Amended and Restated Participation Agreement, dated as of October 6, 2021, by and among Old Saw Mill Holdings LLC, as lessee; the Registrant, as parent guarantor; certain subsidiaries of the Registrant, as subsidiary guarantors; BA Leasing BSC, LLC, as lessor; Bank of America, N.A., as administrative agent; and the lenders party thereto.
10.26	Amended and Restated Lease and Remedies Agreement, dated as of May 2, 2019, between Old Saw Mill Holdings LLC, as lessee, and BA Leasing BSC, LLC, as lessor. (Incorporated by reference from the Form 8-K for the Registrant, filed May 3, 2019.)
10.27	Amended and Restated Guaranty, dated as of May 2, 2019, made by Regeneron Pharmaceuticals, Inc., Regeneron Healthcare Solutions, Inc., and Regeneron Genetics Center LLC, as guarantors. (Incorporated by reference from the Form 8-K for the Registrant, filed May 3, 2019.)
10.28	Letter Agreement, dated as of January 7, 2018, by and among the Registrant, Sanofi, sanofi-aventis US LLC, Aventis Pharmaceuticals Inc., sanofi-aventis Amérique du Nord, and Sanofi Biotechnology SAS. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2018, filed May 3, 2018.)
10.29**	Master Agreement, dated as of April 8, 2019, by and between the Registrant and Alnylam Pharmaceuticals, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2019, filed August 6, 2019.)
10.29.1**	Form of Co-Co Collaboration Agreement (Exhibit B to Master Agreement contained in Exhibit 10.29).
10.29.2**	Form of License Agreement (Exhibit C to Master Agreement contained in Exhibit 10.29).
10.30**	Investor Agreement, dated as of April 8, 2019, by and between the Registrant and Alnylam Pharmaceuticals, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2019, filed August 6, 2019.)
10.31	Stock Purchase Agreement, dated as of April 8, 2019, by and between the Registrant and Alnylam Pharmaceuticals, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended June 30, 2019, filed August 6, 2019.)
10.32	Stock Repurchase Agreement, dated as of May 25, 2020, by and between the Registrant and Sanofi. (Incorporated by reference from the Form 8-K for the Registrant, filed May 29, 2020.)
10.33**	Base Agreement, dated as of July 6, 2020, by and between the Registrant and Advanced Technology International. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2020, filed November 5, 2020.)
10.34**	Project Agreement, dated as of July 6, 2020, by and between the Registrant and Advanced Technology International. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)

10.34.1	Modification No. 01 to Project Agreement, dated as of October 13, 2020, by and between the Registrant and Advanced Technology International. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.34.2**	Modification No. 02 to Project Agreement, dated as of November 17, 2020, by and between the Registrant and Advanced Technology International. (Incorporated by reference from the Form 10-K for the Registrant, for the year ended December 31, 2020, filed February 8, 2021.)
10.35**	License Agreement, dated as of August 18, 2020, by and among the Registrant, F. Hoffman-La Roche Ltd, and Genentech, Inc. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2020, filed November 5, 2020.)
10.36**	Supply Agreement, dated as of January 12, 2021, by and between the Registrant and the U.S. Army Contracting Command, New Jersey. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended March 31, 2021, filed May 6, 2021.)
10.36.1**	Modification P00004 to Supply Agreement, dated as of July 26, 2021, by and between the Registrant and the U.S. Army Contracting Command, New Jersey. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2021, filed November 4, 2021.)
10.36.2**	Modification P00005 to Supply Agreement, dated as of September 14, 2021, by and between the Registrant and the U.S. Army Contracting Command, New Jersey. (Incorporated by reference from the Form 10-Q for the Registrant, for the quarter ended September 30, 2021, filed November 4, 2021.)
21.1	Subsidiaries of the Registrant.
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page of this Annual Report on Form 10-K).
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934.
32	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350.
101	Interactive Data Files pursuant to Rule 405 of Regulation S-T formatted in Inline Extensible Business Reporting Language ("Inline XBRL"): (i) the Registrant's Consolidated Balance Sheets as of December 31, 2021 and 2020; (ii) the Registrant's Consolidated Statements of Operations and Comprehensive Income for the years ended December 31, 2021, 2020, and 2019; (iii) the Registrant's Consolidated Statements of Stockholders' Equity for the years ended December 31, 2021, 2020, and 2019; (iv) the Registrant's Consolidated Statements of Cash Flows for the years ended December 31, 2021, 2020, and 2019; and (v) the notes to the Registrant's Consolidated Financial Statements.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

———

* Portions of this document have been omitted and filed separately with the Commission pursuant to requests for confidential treatment pursuant to Rule 24b-2

** Certain confidential portions of this exhibit were omitted in accordance with Item 601(b)(10) of Regulation S-K

\+ Indicates a management contract or compensatory plan or arrangement

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

REGENERON PHARMACEUTICALS, INC.

Date: February 7, 2022

By: /s/ LEONARD S. SCHLEIFER
Leonard S. Schleifer, M.D., Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Leonard S. Schleifer, President and Chief Executive Officer, and Robert E. Landry, Executive Vice President, Finance and Chief Financial Officer, and each of them, his or her true and lawful attorney-in-fact and agent, with the full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities therewith, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that each said attorney-in-fact and agent, or either of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ LEONARD S. SCHLEIFER Leonard S. Schleifer, M.D., Ph.D.	*President, Chief Executive Officer, and Director (Principal Executive Officer)*	February 7, 2022
/s/ ROBERT E. LANDRY Robert E. Landry	*Executive Vice President, Finance and Chief Financial Officer (Principal Financial Officer)*	February 7, 2022
/s/ CHRISTOPHER R. FENIMORE Christopher R. Fenimore	*Senior Vice President, Controller (Principal Accounting Officer)*	February 7, 2022
/s/ GEORGE D. YANCOPOULOS George D. Yancopoulos, M.D., Ph.D.	*President, Chief Scientific Officer, and Director*	February 7, 2022
/s/ P. ROY VAGELOS P. Roy Vagelos, M.D.	*Chair of the Board of Directors*	February 7, 2022
/s/ BONNIE L. BASSLER Bonnie L. Bassler, Ph.D.	*Director*	February 7, 2022
/s/ MICHAEL S. BROWN Michael S. Brown, M.D.	*Director*	February 7, 2022
/s/ N. ANTHONY COLES N. Anthony Coles, M.D.	*Director*	February 7, 2022
/s/ JOSEPH L. GOLDSTEIN Joseph L. Goldstein, M.D.	*Director*	February 7, 2022
/s/ CHRISTINE A. POON Christine A. Poon	*Director*	February 7, 2022
/s/ ARTHUR F. RYAN Arthur F. Ryan	*Director*	February 7, 2022
/s/ GEORGE L. SING George L. Sing	*Director*	February 7, 2022
/s/ MARC TESSIER-LAVIGNE Marc Tessier-Lavigne, Ph.D.	*Director*	February 7, 2022
/s/ HUDA Y. ZOGHBI Huda Y. Zoghbi, M.D.	*Director*	February 7, 2022

REGENERON PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Regeneron Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Regeneron Pharmaceuticals, Inc. and its subsidiaries (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive income, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2021, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accounting for Other Operating Income related to Research and Development Up-front and Milestone Payments

As described in Note 1 to the consolidated financial statements, other operating income related to collaboration arrangements where the Company satisfies obligations during the development phase over time is typically recognized using an input method on the basis of research and development costs incurred relative to the total expected costs which determines the extent of progress towards completion of the obligation. Other operating income for non-refundable up-front payments and development milestones for which management used an input method, was $42.5 million for the year ended December 31, 2021. As of December 31, 2021, $322.5 million was included in other liabilities representing the amount of previously deferred non-refundable up-front and development milestones expected to be recognized in other operating income over time. Management has disclosed that there is variability in the scope of activities and length of time necessary to develop a drug product, potential delays in development programs, changes to development plans and budgets as programs progress, and uncertainty in the ultimate requirements to obtain governmental approval for commercialization related to these estimates.

The principal considerations for our determination that performing procedures relating to the accounting for other operating income related to research and development up-front and milestone payments is a critical audit matter are the significant judgment by management when determining the estimate of total expected research and development costs to complete the obligation, which in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating evidence to assess the reasonableness of the estimates of the costs to complete.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the accounting for other operating income related to research and development up-front and milestone payments, including controls over the determination of the estimate of total expected research and development costs to complete the obligation. These procedures also included, among others, evaluating and testing management's process for determining the estimate of total expected research and development costs at completion for a sample of contracts, which included evaluating the reasonableness of actual costs incurred and estimated costs to complete. Evaluating the reasonableness of estimated costs to complete involved assessing management's ability to reasonably estimate costs to complete the obligation by (i) obtaining supporting evidence for expected development activities; (ii) evaluating the identification of circumstances that may warrant a modification to estimated costs to complete; and (iii) agreeing estimates of total budgeted costs to contracts or other agreements with collaboration partners.

/s/ PricewaterhouseCoopers LLP

Florham Park, New Jersey
February 7, 2022

We have served as the Company's auditor since 1989.

REGENERON PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(In millions, except share data)

	December 31,	
	2021	**2020**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 2,885.6	$ 2,193.7
Marketable securities	2,809.1	1,393.3
Accounts receivable, net	6,036.5	4,114.7
Inventories	1,951.3	1,916.6
Prepaid expenses and other current assets	332.4	160.8
Total current assets	14,014.9	9,779.1
Marketable securities	6,838.0	3,135.6
Property, plant, and equipment, net	3,482.2	3,221.6
Deferred tax assets	876.9	858.9
Other noncurrent assets	222.8	168.1
Total assets	$ 25,434.8	$ 17,163.3
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 564.0	$ 475.5
Accrued expenses and other current liabilities	2,206.8	1,644.2
Finance lease liabilities	719.7	—
Deferred revenue	442.0	577.7
Total current liabilities	3,932.5	2,697.4
Long-term debt	1,980.0	1,978.5
Finance lease liabilities	—	717.2
Deferred revenue	73.3	57.8
Other noncurrent liabilities	680.2	687.1
Total liabilities	6,666.0	6,138.0
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Preferred Stock, $.01 par value; 30,000,000 shares authorized; issued and outstanding - none	—	—
Class A Stock, convertible, $.001 par value; 40,000,000 shares authorized; shares issued and outstanding - 1,823,283 in 2021 and 1,848,970 in 2020	—	—
Common Stock, $.001 par value; 320,000,000 shares authorized; shares issued - 126,244,444 in 2021 and 121,533,460 in 2020	0.1	0.1
Additional paid-in capital	8,087.5	6,716.2
Retained earnings	18,968.3	10,893.0
Accumulated other comprehensive (loss) income	(26.2)	29.3
Treasury Stock, at cost; 19,392,961 shares in 2021 and 16,431,520 shares in 2020	(8,260.9)	(6,613.3)
Total stockholders' equity	18,768.8	11,025.3
Total liabilities and stockholders' equity	$ 25,434.8	$ 17,163.3

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME
(In millions, except per share data)

	Year Ended December 31,		
	2021	**2020**	**2019**
Statements of Operations			
Revenues:			
Net product sales	$ 12,117.2	$ 5,567.6	$ 4,834.4
Sanofi collaboration revenue	1,902.2	1,186.4	403.6
Other collaboration revenue	1,771.1	1,186.1	1,145.6
Other revenue	281.2	557.0	174.0
	16,071.7	8,497.1	6,557.6
Expenses:			
Research and development	2,908.1	2,735.0	2,450.0
Selling, general, and administrative	1,824.9	1,346.0	1,341.9
Cost of goods sold	1,773.1	491.9	362.3
Cost of collaboration and contract manufacturing	664.4	628.0	402.8
Other operating (income) expense, net	(45.6)	(280.4)	(209.2)
	7,124.9	4,920.5	4,347.8
Income from operations	8,946.8	3,576.6	2,209.8
Other income (expense):			
Other income (expense), net	436.3	290.7	249.5
Interest expense	(57.3)	(56.9)	(30.2)
	379.0	233.8	219.3
Income before income taxes	9,325.8	3,810.4	2,429.1
Income tax expense	1,250.5	297.2	313.3
Net income	$ 8,075.3	$ 3,513.2	$ 2,115.8
Net income per share - basic	$ 76.40	$ 32.65	$ 19.38
Net income per share - diluted	$ 71.97	$ 30.52	$ 18.46
Weighted average shares outstanding - basic	105.7	107.6	109.2
Weighted average shares outstanding - diluted	112.2	115.1	114.6
Statements of Comprehensive Income			
Net income	$ 8,075.3	$ 3,513.2	$ 2,115.8
Other comprehensive income (loss), net of tax:			
Unrealized (loss) gain on debt securities	(56.4)	9.1	35.9
Unrealized gain (loss) on cash flow hedges	0.9	(0.9)	(2.5)
Comprehensive income	$ 8,019.8	$ 3,521.4	$ 2,149.2

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
For the Years Ended December 31, 2021, 2020, and 2019
(In millions)

	Class A Stock		Common Stock		Additional Paid-in Capital	Retained Earnings	Accumulated Other Comprehensive Income (Loss)	Treasury Stock		Total Stockholders' Equity
	Shares	Amount	Shares	Amount				Shares	Amount	
Balance, December 31, 2018	1.9	—	111.1	$ 0.1	$ 3,911.6	$ 5,254.3	$ (12.3)	(4.0)	$ (396.4)	$ 8,757.3
Issuance of Common Stock for equity awards granted under long-term incentive plans	—	—	2.6	—	213.2	—	—	—	—	213.2
Common Stock tendered upon exercise of stock options and vesting of restricted stock for employee tax obligations	—	—	(0.5)	—	(188.0)	—	—	—	—	(188.0)
Issuance/distribution of Common Stock for 401(k) Savings Plan	—	—	—	—	24.9	—	—	0.1	13.2	38.1
Repurchases of Common Stock	—	—	—	—	—	—	—	(1.0)	(356.7)	(356.7)
Conversion of Class A Stock to Common Stock	(0.1)	—	0.1	—	—	—	—	—	—	—
Stock-based compensation charges	—	—	—	—	466.9	—	—	—	—	466.9
Adjustment upon adoption of new accounting standard	—	—	—	—	—	9.7	—	—	—	9.7
Net income	—	—	—	—	—	2,115.8	—	—	—	2,115.8
Other comprehensive income, net of tax	—	—	—	—	—	—	33.4	—	—	33.4
Balance, December 31, 2019	1.8	—	113.3	0.1	4,428.6	7,379.8	21.1	(4.9)	(739.9)	11,089.7
Issuance of Common Stock for equity awards granted under long-term incentive plans	—	—	9.6	—	2,576.4	—	—	—	—	2,576.4
Common Stock tendered upon exercise of stock options and vesting of restricted stock for employee tax obligations	—	—	(1.4)	—	(768.9)	—	—	—	—	(768.9)
Issuance/distribution of Common Stock for 401(k) Savings Plan	—	—	—	—	37.2	—	—	0.1	7.5	44.7
Repurchases of Common Stock	—	—	—	—	—	—	—	(11.6)	(5,880.9)	(5,880.9)
Stock-based compensation charges	—	—	—	—	442.9	—	—	—	—	442.9
Net income	—	—	—	—	—	3,513.2	—	—	—	3,513.2
Other comprehensive income, net of tax	—	—	—	—	—	—	8.2	—	—	8.2
Balance, December 31, 2020	1.8	—	121.5	0.1	6,716.2	10,893.0	29.3	(16.4)	(6,613.3)	11,025.3

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY *(continued)*

	Class A Stock		Common Stock		Additional Paid-in Capital	Retained Earnings	Accumulated Other Comprehensive Income (Loss)	Treasury Stock		Total Stockholders' Equity
	Shares	Amount	Shares	Amount				Shares	Amount	
Issuance of Common Stock for equity awards granted under long-term incentive plans	—	—	6.2	—	1,676.0	—	—	—	—	1,676.0
Common Stock tendered upon exercise of stock options and vesting of restricted stock for employee tax obligations	—	—	(1.5)	—	(944.6)	—	—	—	—	(944.6)
Issuance/distribution of Common Stock for 401(k) Savings Plan	—	—	—	—	40.7	—	—	0.1	7.4	48.1
Repurchases of Common Stock	—	—	—	—	—	—	—	(3.1)	(1,655.0)	(1,655.0)
Stock-based compensation charges	—	—	—	—	599.2	—	—	—	—	599.2
Net income	—	—	—	—	—	8,075.3	—	—	—	8,075.3
Other comprehensive loss, net of tax	—	—	—	—	—	—	(55.5)	—	—	(55.5)
Balance, December 31, 2021	1.8	—	126.2	$ 0.1	$ 8,087.5	$ 18,968.3	$ (26.2)	(19.4)	$ (8,260.9)	$ 18,768.8

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In millions)

	Year Ended December 31,		
	2021	**2020**	**2019**
Cash flows from operating activities:			
Net income	$ 8,075.3	$ 3,513.2	$ 2,115.8
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	286.2	235.9	210.3
Non-cash compensation expense	601.7	432.0	464.3
Gains on marketable and other securities, net	(387.0)	(221.8)	(131.5)
Other non-cash items, net	568.7	86.8	102.2
Deferred taxes	(147.1)	75.6	(130.6)
Changes in assets and liabilities:			
Increase in accounts receivable	(1,927.4)	(1,356.1)	(523.7)
Increase in inventories	(494.3)	(529.4)	(335.5)
(Increase) decrease in prepaid expenses and other assets	(240.7)	114.9	(79.8)
(Decrease) increase in deferred revenue	(120.2)	148.1	139.5
Increase in accounts payable, accrued expenses, and other liabilities	866.1	118.9	599.0
Total adjustments	(994.0)	(895.1)	314.2
Net cash provided by operating activities	7,081.3	2,618.1	2,430.0
Cash flows from investing activities:			
Purchases of marketable and other securities	(7,048.1)	(3,241.0)	(3,202.4)
Sales or maturities of marketable and other securities	2,215.3	3,785.0	1,604.2
Capital expenditures	(551.9)	(614.6)	(429.6)
Net cash used in investing activities	(5,384.7)	(70.6)	(2,027.8)
Cash flows from financing activities:			
Proceeds from issuance of Common Stock	1,672.3	2,575.2	211.8
Payments in connection with Common Stock tendered for employee tax obligations	(1,032.7)	(680.8)	(188.0)
Repurchases of Common Stock	(1,645.4)	(5,846.8)	(275.9)
Proceeds from issuance of long-term debt	—	1,981.9	—
Proceeds from bridge loan facility	—	1,500.0	—
Repayment of bridge loan facility	—	(1,500.0)	—
Net cash used in financing activities	(1,005.8)	(1,970.5)	(252.1)
Net increase in cash, cash equivalents, and restricted cash	690.8	577.0	150.1
Cash, cash equivalents, and restricted cash at beginning of period	2,207.3	1,630.3	1,480.2
Cash, cash equivalents, and restricted cash at end of period	$ 2,898.1	$ 2,207.3	$ 1,630.3
Supplemental disclosure of cash flow information			
Cash paid for interest (net of amounts capitalized)	$ 55.8	$ 23.2	$ 25.0
Cash paid for income taxes	$ 1,218.4	$ 188.1	$ 342.3

The accompanying notes are an integral part of the financial statements.

1. Business Overview and Summary of Significant Accounting Policies

Organization and Business

Regeneron Pharmaceuticals, Inc. and its subsidiaries ("Regeneron," "Company," "we," "us," and "our") is a fully integrated biotechnology company that discovers, invents, develops, manufactures, and commercializes medicines for serious diseases. Our commercialized medicines and product candidates in development are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematologic conditions, infectious diseases, and rare diseases. We currently have nine products that have received marketing approval by the U.S. Food and Drug Administration ("FDA"). In addition, REGEN-COV® has not been approved by the FDA, but has been authorized under an Emergency Use Authorization ("EUA") (see Note 3 and Note 6 for additional information). The Company is a party to collaboration agreements to develop and commercialize, as applicable, certain products and product candidates (see Note 3).

The Company operates in one business segment, which includes all activities related to the discovery, development, and commercialization of medicines for serious diseases. The Company's business is subject to certain risks including, but not limited to, uncertainties relating to conducting research activities, product development, obtaining regulatory approvals, competition, and obtaining and enforcing patents.

Basis of Presentation

The consolidated financial statements include the accounts of Regeneron and its wholly-owned subsidiaries. Intercompany balances and transactions are eliminated in consolidation. Certain reclassifications have been made to prior period amounts to conform with the current period's presentation.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. The extent to which the COVID-19 pandemic may directly or indirectly impact our business, financial condition, and results of operations is highly uncertain and subject to change. We considered the potential impact of the COVID-19 pandemic on our estimates and assumptions and, other than the inventory write-offs and reserves recorded related to REGEN-COV (see Note 6), there was not a material impact to our consolidated financial statements as of and for the year ended December 31, 2021; however, actual results could differ from those estimates and there may be changes to our estimates in future periods.

Concentration of Credit Risk

Financial instruments which potentially expose the Company to concentrations of credit risk consist of cash, cash equivalents, certain investments, and accounts receivable. In accordance with the Company's policies, the Company mandates asset diversification and monitors exposure with its counterparties.

Concentrations of credit risk with respect to customer and collaborator accounts receivable are significant. As of December 31, 2021, three individual customers accounted for 91% (including 29% related to the U.S. government) of the Company's net trade accounts receivable balances. Three individual customers accounted for 93% of the Company's net trade accounts receivable balances as of December 31, 2020. The Company has contractual payment terms with each of its collaborators and customers, and the Company monitors their financial performance and credit worthiness so that it can properly assess and respond to any changes in their credit profile. As of December 31, 2021 and 2020, there were no write-offs and allowances of accounts receivable related to credit risk for our collaborators or customers.

Significant Accounting Policies

Cash and Cash Equivalents

The Company considers all highly liquid debt instruments with a maturity of three months or less when purchased to be cash equivalents. The carrying amount reported in the Consolidated Balance Sheet for cash and cash equivalents approximates its fair value.

Debt and Equity Securities

The Company has an investment policy that includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and diversification. We invest our cash primarily in debt securities. We consider our investments in debt securities to be "available-for-sale," as defined by authoritative guidance issued by the Financial Accounting Standards Board ("FASB"). These assets are carried at fair value and the unrealized gains and losses are included in accumulated other comprehensive income (loss). Realized gains and losses on available-for-sale debt securities are included in other income (expense), net. The Company reviews its portfolio of available-for-sale debt securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost have resulted from a credit-related loss or other factors. If the decline in fair value is due to credit-related factors, a loss is recognized in net income, whereas if the decline in fair value is not due to credit-related factors, the loss is recorded in other comprehensive income (loss).

We also have investments in equity securities that are carried at fair value with changes in fair value recognized within other income (expense), net. We have elected to measure certain equity investments we hold that do not have readily determinable fair values at cost less impairment, if any, and adjust for observable price changes in orderly transactions for identical or similar investments of the same issuer within other income (expense), net.

Accounts Receivable

The Company's trade accounts receivable arise from product sales and represent amounts due from its customers, which are all located in the United States. In addition, the Company records accounts receivable arising from its collaboration and licensing agreements. The Company monitors the financial performance and credit worthiness of its counterparties so that it can properly assess and respond to changes in their credit profile. The Company provides allowances against receivables for estimated losses, if any, that may result from a counterparty's inability to pay. Amounts determined to be uncollectible are written-off against the allowance.

Inventories

Inventories are stated at the lower of cost or net realizable value. The Company determines the cost of inventory using the first-in, first-out, or FIFO, method.

The Company capitalizes inventory costs associated with the Company's products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns, potential labeling restrictions, and any other impediments to obtaining regulatory approval.

The Company periodically analyzes its inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, and writes down such inventories as appropriate. In addition, the Company's products are subject to strict quality control and monitoring which the Company performs throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, the Company records a charge to write down such inventory to its estimated realizable value.

Property, Plant, and Equipment

Property, plant, and equipment are stated at cost, net of accumulated depreciation. Depreciation is calculated on a straight-line basis over the estimated useful lives of the assets. Leasehold improvements are amortized over the shorter of the estimated useful lives of the assets or the remaining lease term. Costs of construction of certain long-lived assets include capitalized interest, which is amortized over the estimated useful life of the related asset. Expenditures for maintenance and repairs which do not materially extend the useful lives of the assets are charged to expense as incurred. The cost and accumulated depreciation or amortization of assets retired or sold are removed from the respective accounts, and any gain or loss is recognized in income (loss) from operations. The estimated useful lives of property, plant, and equipment are as follows:

Building and improvements	10–50 years
Laboratory and other equipment	3–10 years
Furniture and fixtures	5 years

The Company periodically assesses the recoverability of long-lived assets, such as property, plant, and equipment, and evaluates such assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

Leases

The Company determines if an arrangement is a lease considering whether there is an identified asset and the contract conveys the right to control its use. Leases with an initial term of 12 months or less are not recorded on the balance sheet. The Company's lease terms may include options to extend or terminate a lease when it is reasonably certain that it will exercise that option. The Company accounts for lease components (e.g., rental payments) separately from non-lease components (e.g., common area maintenance costs).

Right-of-use assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term, unless there is a transfer of title or purchase option we are reasonably certain to exercise. For leases where an implicit rate is not readily determinable, we use our incremental borrowing rate based on information available at the lease commencement date to determine the present value of future lease payments. Lease expense for operating leases is recognized on a straight-line basis over the expected lease term.

Revenue Recognition - Product Revenue

Revenue from product sales is recognized at a point in time when our customer is deemed to have obtained control of the product, which generally occurs upon receipt or acceptance by our customer.

The amount of revenue we recognize from product sales may vary due to rebates, chargebacks, and discounts provided under governmental and other programs, distribution-related fees, and other sales-related deductions. In order to determine the transaction price, we estimate, utilizing the expected value method, the amount of variable consideration to which we will be entitled. This estimate is based upon contracts with customers, healthcare providers, payors, and government agencies, statutorily-defined discounts applicable to government-funded programs, historical experience, estimated payor mix, and other relevant factors. The Company reviews its estimates of rebates, chargebacks, and other applicable provisions each period and records any necessary adjustments in the current period's net product sales.

- *Rebates:* The Company’s rebates include amounts paid to managed care organizations, group purchasing organizations, state Medicaid programs, and other rebate programs. The Company estimates reductions to product sales for each type of rebate and records an allowance for rebates in the same period in which the related product sales are recognized. The Company’s liability for rebates consists of estimates for claims related to the current and prior periods that have not been paid and estimates for claims that will be made related to inventory that exists in the distribution channel at the end of the period.
- *Chargebacks and Discounts:* The Company's reserves related to discounted pricing to eligible physicians, Veterans' Administration ("VA"), Public Health Services, and others (collectively "qualified healthcare providers") represent the Company's estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices the Company charges to its customers (i.e., distributors and specialty pharmacies). The Company's customers charge the Company for the difference between what they pay for the products and the discounted selling price to the qualified healthcare providers. The Company estimates reductions to product sales for each type of chargeback and records an allowance for chargebacks in the same period that the related product sales are recognized. The Company's reserve for chargebacks consists of amounts for which we expect to issue credit based on expected sales by our customers to qualified healthcare providers and chargebacks that customers have claimed but for which we have not yet issued credit.
- *Distribution-Related Fees:* The Company has written contracts with its customers that include terms for distribution-related fees. The Company estimates and records distribution and related fees due to its customers generally based on gross sales.
- *Other Sales-Related Deductions*: The Company's other sales-related deductions include co-pay assistance programs and product returns. The Company estimates and records other sales-related deductions generally based on gross sales, written contracts, and other relevant factors.

Consistent with industry practice, the Company offers its customers a limited right to return product purchased directly from the Company, which is principally based upon the product's expiration date. Product returned is generally not resalable given the nature of the Company's products and method of administration. The Company develops estimates for product returns based upon historical experience, shelf life of the product, and other relevant factors. The Company monitors product supply levels in the distribution channel, as well as sales by its customers, using product-specific data provided by its customers. If necessary, the Company's estimates of product returns may be adjusted in the future based on actual returns experience, known or expected changes in the marketplace, or other factors.

Collaborative Arrangements

We have entered into various collaborative arrangements to research, develop, manufacture, and commercialize products and/or product candidates. Although each of these arrangements is unique in nature, such arrangements involve a joint operating activity where both parties are active participants in the activities of the collaboration and exposed to significant risks and rewards dependent on the commercial success of the activities.

In arrangements where we do not deem our collaborator to be our customer, payments to and from our collaborator are presented in our statement of operations based on the nature of our business operations, the nature of the arrangement, including the contractual terms, and the nature of the payments, as summarized in the table and further described below.

Nature/Type of Payment	Statement of Operations Presentation
Regeneron's share of profits or losses in connection with commercialization of products	Collaboration revenue
Reimbursement for manufacturing of commercial supplies	Collaboration revenue
Royalties and/or sales-based milestones earned	Collaboration revenue
Reimbursement of Regeneron's research and development expenses	Reduction to Research and development expenses
Regeneron's obligation for its share of collaborator's research and development expenses	Research and development expense
Up-front and development milestone payments to collaborators	Research and development expense
Reimbursement of Regeneron's commercialization-related expenses	Reduction to Selling, general, and administrative expense
Regeneron's obligation for its share of collaborator's commercialization-related expenses	Selling, general, and administrative expense
Regeneron's obligation to pay collaborator for its share of gross profits when Regeneron is deemed to be the principal	Cost of goods sold
Up-front and development milestones earned (when we have a combined unit of account which includes a license and providing research and development services)	Other operating income

In agreements involving multiple goods or services promised to be transferred to our collaborator, we must assess, at the inception of the contract, whether each promise represents a separate obligation (i.e., is "distinct"), or whether such promises should be combined as a single unit of account. When we have a combined unit of account which includes a license and providing research and development services to our collaborator, recognition of up-front payments and development milestones earned from our collaborator is deferred (as a liability) and recognized over the development period (i.e., over time). In arrangements where we satisfy our obligation(s) during the development phase over time, we recognize amounts initially deferred over time typically using an input method on the basis of our research and development costs incurred relative to the total expected cost which determines the extent of our progress toward completion. We review our estimates each period and make revisions to such estimates as necessary. We recognized other operating income in connection with non-refundable up-front and development milestones previously received, for which we used an input method, of $42.5 million and $276.7 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, $322.5 million was included in other liabilities representing the amount of previously deferred non-refundable up-front and development milestones expected to be recognized in other operating income over time.

When we are entitled to reimbursement of all or a portion of the expenses (e.g., research and development expenses) that we incur under a collaboration, we record those reimbursable amounts in the period in which such costs are incurred.

If our collaborator performs research and development work or commercialization-related activities and share costs, we also recognize, as expense (e.g., research and development expense or selling, general, and administrative expense, as applicable) in the period when our collaborator incurs such expenses, the portion of the collaborator's expenses that we are obligated to reimburse. Our collaborators provide us with estimated expenses for the most recent fiscal quarter. The estimates are revised, if necessary, in subsequent periods if actual expenses differ from those estimates.

Under certain of the Company's collaboration agreements, product sales and cost of sales may be recorded by the Company's collaborators as they are deemed to be the principal in the transaction. In arrangements where we:

- supply commercial product to our collaborator, we may be reimbursed for our manufacturing costs as commercial product is shipped to the collaborator; however, recognition of such cost reimbursements may be deferred until the product is sold by our collaborator to third-party customers;
- share in any profits or losses arising from the commercialization of such products, we record our share of the variable consideration, representing net product sales less cost of goods sold and shared commercialization and other expenses, in the period in which such underlying sales occur and costs are incurred by the collaborator; and
- receive royalties and/or sales-based milestone payments from our collaborator, we recognize such amounts in the period earned.

Our collaborators provide us with estimates of product sales and our share of profits or losses, as applicable, for each quarter. The estimates are revised, if necessary, in subsequent periods if our actual share of profits or losses differ from those estimates.

Research and Development Expenses

Research and development expenses include costs attributable to the conduct of research and development programs, including the cost of salaries, payroll taxes, employee benefits, materials, supplies, depreciation on and maintenance of research equipment, costs related to research collaboration and licensing agreements, clinical trial expenses, the cost of services provided by outside contractors, including services related to the Company's clinical trials, the full cost of manufacturing drug for use in research and development, amounts that the Company is obligated to reimburse to collaborators for research and development expenses that they incur, and the allocable portions of facility costs. Costs associated with research and development are expensed.

For each clinical trial that we conduct, certain clinical trial costs are expensed immediately, while others are expensed over time based on the expected total number of patients in the trial, the rate at which patients enter and remain in the trial, and/or the period over which clinical investigators, contract research organizations ("CROs"), or other third-party service providers are expected to provide services. In the event of early termination of a clinical trial, we accrue and recognize expenses in an amount based on our estimate of the remaining noncancelable obligations associated with the winding-down of the clinical trial, including any applicable penalties.

Stock-based Compensation

The Company recognizes stock-based compensation expense for equity grants under the Company's long-term incentive plans to employees and non-employee members of the Company's board of directors (as applicable) based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period.

The fair value of stock option awards is estimated using the Black-Scholes model. Stock-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The fair value of performance-based restricted stock units which are subject to vesting based on the Company’s attainment of pre-established market performance goals is estimated using a Monte Carlo simulation. The probability of the number of actual shares expected to be earned is considered in the grant-date valuation, and therefore, stock-based compensation expense is not adjusted at the vesting date to reflect the actual number of shares earned.

Income Taxes

The provision for income taxes includes U.S. federal, state, local, and foreign taxes. Income taxes are accounted for under the liability method. Deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns, including deferred tax assets and liabilities for expected amounts of global intangible low-taxed income ("GILTI") inclusions, are recognized on the difference between the tax basis of assets and liabilities and their respective financial reporting amounts ("temporary differences") at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets will not be realized.

Uncertain tax positions, for which management's assessment is that there is more than a 50% probability that the position will be sustained upon examination by a taxing authority based upon its technical merits, are subjected to certain recognition and measurement criteria. The Company re-evaluates uncertain tax positions and considers various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, and changes in facts or circumstances related to a tax position. The Company adjusts the amount of the liability to reflect any subsequent changes in the

relevant facts and circumstances surrounding the uncertain positions. The Company recognizes interest and penalties related to income tax matters in income tax expense.

Per Share Data

Basic net income per share is computed by dividing net income by the weighted average number of shares of Common Stock and Class A Stock outstanding. Net income per share is presented on a combined basis, inclusive of Common Stock and Class A Stock outstanding, as each class of stock has equivalent economic rights. Basic net income per share excludes restricted stock until vested. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were converted or exercised during the period, when the effect is dilutive. Common stock equivalents include: (i) outstanding stock options and unvested restricted stock under the Company's long-term incentive plans, which are included under the treasury stock method when dilutive, and (ii) Common Stock that would be issued upon the achievement of certain market conditions, which are included under the treasury stock method when dilutive.

2. Product Sales

Net product sales consist of the following:

(In millions)	Year Ended December 31,		
Net Product Sales in the United States	**2021**	**2020**	**2019**
EYLEA®	$ 5,792.3	$ 4,947.2	$ 4,644.2
Libtayo®	306.3	270.7	175.7
Praluent®	170.0	150.9 *	*
REGEN-COV***	5,828.0	185.7	—
Evkeeza®	18.4	—	—
ARCALYST®	2.2 **	13.1	14.5
	$ 12,117.2	$ 5,567.6	$ 4,834.4

* Effective April 1, 2020, the Company became solely responsible for the development and commercialization of Praluent in the United States and records net product sales of Praluent in the United States. Previously, Sanofi recorded net product sales of Praluent in the United States. See Note 3 for further details.

** Effective April 1, 2021, Kiniksa records net product sales of ARCALYST in the United States. Previously, the Company recorded net product sales of ARCALYST in the United States.

*** Net product sales of REGEN-COV in the United States relate to product sold in connection with our agreements with the U.S. government. See Note 3 for further details.

As of December 31, 2021 and 2020, the Company had $5.059 billion and $3.112 billion, respectively, of trade accounts receivable that were recorded within Accounts receivable, net.

The Company had product sales to certain customers that accounted for more than 10% of total gross product revenue for each of the years ended December 31, 2021, 2020, and 2019. Sales to each of these customers as a percentage of the Company's total gross product revenue are as follows:

	Year Ended December 31,		
	2021	**2020**	**2019**
Besse Medical, a subsidiary of AmerisourceBergen Corporation	30 %	51 %	57 %
McKesson Corporation	18 %	32 %	33 %
U.S. government	43 %	*	—

* Sales to the U.S. government represented less than 10% of total gross product revenue during the period

Revenue from product sales is recorded net of applicable provisions for rebates, chargebacks, and discounts, distribution-related fees, and other sales-related deductions. Accruals for chargebacks and discounts are recorded as a direct reduction to accounts receivable. Accruals for rebates, distribution-related fees, and other sales-related deductions are recorded within accrued liabilities. The following table summarizes the provisions, and credits/payments, for sales-related deductions.

(In millions)	Rebates, Chargebacks, and Discounts	Distribution-Related Fees	Other Sales-Related Deductions	Total
Balance as of December 31, 2018	$ 41.1	$ 42.0	$ 8.3	$ 91.4
Provisions	423.2	242.9	61.8	727.9
Credits/payments	(384.0)	(238.5)	(40.7)	(663.2)
Balance as of December 31, 2019	80.3	46.4	29.4	156.1
Provisions	762.9	279.9	94.1	1,136.9
Credits/payments	(641.0)	(249.1)	(78.7)	(968.8)
Balance as of December 31, 2020	202.2	77.2	44.8	324.2
Provisions	1,047.1	363.6	150.4	1,561.1
Credits/payments	(1,034.7)	(360.8)	(127.6)	(1,523.1)
Balance as of December 31, 2021	$ 214.6	$ 80.0	$ 67.6	$ 362.2

3. Collaboration, License, and Other Agreements

a. Sanofi

Amounts recognized in our Statements of Operations in connection with our collaborations with Sanofi are detailed below:

(In millions)	Statement of Operations Classification	Year Ended December 31, 2021	2020	2019
Antibody:				
Regeneron's share of profits in connection with commercialization of antibodies	Sanofi collaboration revenue	$ 1,363.0	$ 785.2	$ 209.3
Sales-based milestones earned	Sanofi collaboration revenue	$ 50.0	$ 50.0	—
Reimbursement for manufacturing of commercial supplies	Sanofi collaboration revenue	$ 488.8	$ 368.0	$ 216.0
Reimbursement of research and development expenses	Reduction of Research and development expense	$ 175.9	$ 226.7	$ 277.7
Regeneron's obligation for its share of Sanofi research and development expenses	Research and development expense	$ (46.7)	$ (77.6)	$ (46.0)
Reimbursement of commercialization-related expenses	Reduction of Selling, general, and administrative expense	$ 320.5	$ 359.4	$ 479.9
Immuno-oncology:				
Regeneron's share of losses in connection with commercialization of Libtayo outside the United States	Sanofi collaboration revenue	$ (13.6)	$ (25.7)	$ (21.7)
Reimbursement for manufacturing of commercial supplies	Sanofi collaboration revenue	$ 14.0	$ 8.9	—
Reimbursement of research and development expenses	Reduction of Research and development expense	$ 85.1	$ 166.2	$ 163.0
Reimbursement of commercialization-related expenses	Reduction of Selling, general, and administrative expense	$ 89.6	$ 64.7	$ 10.3
Regeneron's obligation for its share of Sanofi commercial expenses	Selling, general, and administrative expense	$ (36.3)	$ (22.4)	$ (15.4)
Regeneron's obligation for Sanofi's share of Libtayo U.S. gross profits	Cost of goods sold	$ (133.0)	$ (119.1)	$ (78.2)
Amounts recognized in connection with up-front payments received	Other operating income	$ 6.1	$ 210.6	$ 92.7

Antibody

The Company is party to a global, strategic collaboration with Sanofi to research, develop, and commercialize fully human monoclonal antibodies (the "Antibody Collaboration"), which currently consists of Dupixent®, Kevzara®, and itepekimab. Under the terms of the Antibody License and Collaboration Agreement ("LCA"), Sanofi is generally responsible for funding 80%–100% of agreed-upon development costs. We are obligated to reimburse Sanofi for 30%–50% of worldwide development expenses that were funded by Sanofi (collectively, the "development balance") based on our share of collaboration profits from commercialization of collaboration products. However, we are only required to apply 10% of our share of the profits from the Antibody Collaboration in any calendar quarter to reimburse Sanofi for these development costs. The Company's contingent reimbursement obligation (development balance) to Sanofi under the Antibody Collaboration was approximately $3.152 billion as of December 31, 2021.

Effective January 2018, the Company and Sanofi entered into a letter agreement (the "Letter Agreement") in connection with, among other matters, the allocation of additional funds to certain activities relating to dupilumab and itepekimab (collectively, the "Dupilumab/Itepekimab Eligible Investments"). Refer to the "*Immuno-Oncology*" section below for further details regarding the Letter Agreement and Note 11 for additional information regarding shares purchased by us from Sanofi.

Sanofi leads commercialization activities for products under the Antibody Collaboration, subject to the Company's right to co-commercialize such products. The Company co-commercializes Dupixent in the United States and in certain countries outside the United States. The parties equally share profits and losses from sales within the United States. The parties share profits outside the United States on a sliding scale based on sales starting at 65% (Sanofi)/35% (Regeneron) and ending at 55% (Sanofi)/45% (Regeneron), and losses outside the United States at 55% (Sanofi)/45% (Regeneron).

In addition to profit and loss sharing, the Company is entitled to receive sales milestone payments from Sanofi. In each of 2020 and 2021, the Company earned, and recognized as revenue, a $50.0 million sales-based milestone from Sanofi, upon aggregate annual sales of antibodies outside the United States (including Praluent) exceeding $1.0 billion and $1.5 billion, respectively, on a rolling twelve-month basis. We are entitled to receive up to an aggregate of $150.0 million in additional sales milestone payments from Sanofi, which includes the next sales milestone payment of $50.0 million that would be earned when such sales outside the United States exceed $2.0 billion on a rolling twelve-month basis.

In April 2020, the Company and Sanofi entered into an amendment to the LCA in connection with, among other things, the removal of Praluent from the LCA such that (i) effective April 1, 2020, the LCA no longer governs the development, manufacture, or commercialization of Praluent and (ii) the quarterly period ended March 31, 2020 was the last quarter for which Sanofi and the Company shared profits and losses for Praluent under the LCA. The parties also entered into a Praluent Cross License & Commercialization Agreement (the "Praluent Agreement") pursuant to which, effective April 1, 2020, the Company, at its sole cost, became solely responsible for the development and commercialization of Praluent in the United States, and Sanofi, at its sole cost, became solely responsible for the development and commercialization of Praluent outside of the United States. Under the Praluent Agreement, Sanofi will pay the Company a 5% royalty on Sanofi’s net product sales of Praluent outside the United States until March 31, 2032. The Company will not owe Sanofi royalties on the Company’s net product sales of Praluent in the United States. Although each party will be responsible for manufacturing Praluent for its respective territory, the parties have entered into definitive supply agreements under which, for a certain transitional period, the Company will continue to supply drug substance to Sanofi and Sanofi will continue to supply finished product to Regeneron. With respect to any intellectual property or product liability litigation relating to Praluent, the parties have agreed that, effective April 1, 2020, Regeneron and Sanofi each will be solely responsible for any such litigation (including damages and other costs and expenses thereof) in the United States and outside the United States, respectively, arising out of Praluent sales or other activities on or after April 1, 2020 (subject to Sanofi's right to set off a portion of any third-party royalty payments resulting from certain patent litigation proceedings against up to 50% of any Praluent royalty payment owed to Regeneron). The parties will each bear 50% of any damages arising out of Praluent sales or other activities prior to April 1, 2020. See Note 15 for discussion of legal proceedings related to Praluent.

The Company's significant promised goods and services in connection with the Antibody Collaboration consist of providing research and development services, including the manufacturing of clinical supplies, and providing commercial-related services, including the manufacturing of commercial supplies. We recognize amounts in connection with the Antibody Collaboration based on the amount we have the right to invoice and such amount corresponds directly with our performance to date; therefore, we do not disclose the value of the transaction price (i.e., the amount of consideration we expect to be entitled to) allocated to our remaining unsatisfied obligations.

The following table summarizes contract balances in connection with the Company's Antibody Collaboration with Sanofi:

	As of December 31,	
(In millions)	**2021**	**2020**
Accounts receivable, net	$ 504.8	$ 407.7
Deferred revenue	$ 368.7	$ 347.7

Immuno-Oncology

The Company is party to a collaboration with Sanofi to research, develop, and commercialize antibody-based cancer treatments in the field of immuno-oncology (the "IO Collaboration"). The IO Collaboration is governed by an Amended and Restated Immuno-oncology Discovery and Development Agreement ("Amended IO Discovery Agreement"), and an Immuno-oncology License and Collaboration Agreement ("IO License and Collaboration Agreement"). In connection with the execution of the original Immuno-oncology Discovery and Development Agreement in 2015 ("2015 IO Discovery Agreement"), which has been replaced by the Amended IO Discovery Agreement (as discussed below), Sanofi made a $265.0 million non-refundable up-front payment to the Company. Pursuant to the 2015 IO Discovery Agreement, the Company was to identify and validate potential immuno-oncology targets and develop therapeutic antibodies against such targets through clinical proof-of-concept.

We are obligated to reimburse Sanofi for half of the development costs it funded that are attributable to clinical development of antibody product candidates from our share of future profits from commercialized IO Collaboration products. However, the Company is only required to apply 10% of its share of the profits from IO Collaboration products in any calendar quarter towards reimbursing Sanofi for these development costs. The Company's contingent reimbursement obligation to Sanofi under the IO Collaboration was approximately $103 million as of December 31, 2021.

Effective December 31, 2018, the Company and Sanofi entered into the Amended IO Discovery Agreement, which narrowed the scope of the existing discovery and development activities conducted by the Company ("IO Development Activities") under the 2015 IO Discovery Agreement to developing therapeutic bispecific antibodies targeting (i) BCMA and CD3 (the "BCMAxCD3 Program") and (ii) MUC16 and CD3 (the "MUC16xCD3 Program") through clinical proof-of-concept. The Amended IO Discovery Agreement provided for Sanofi’s payment of $461.9 million to the Company as consideration for (x) the termination of the 2015 IO Discovery Agreement, (y) the prepayment for certain IO Development Activities regarding the BCMAxCD3 Program and the MUC16xCD3 Program, and (z) the reimbursement of costs incurred by the Company under the 2015 IO Discovery Agreement during the fourth quarter of 2018.

Under the terms of the Amended IO Discovery Agreement, the Company was required to conduct development activities with respect to (i) the BCMAxCD3 Program through the earlier of clinical proof-of-concept or the expenditure of $70.0 million and (ii) the MUC16xCD3 Program through the earlier of clinical proof-of-concept or the expenditure of $50.0 million. During the first quarter of 2021, Sanofi did not exercise its options to license rights to these product candidates; as a result, we retain the exclusive right to develop and commercialize such product candidates and Sanofi will receive a royalty on sales (if any). In addition, the Company has no further obligations to develop drug product candidates under the Amended IO Discovery Agreement.

In connection with the execution of the IO License and Collaboration Agreement in 2015, Sanofi made a $375.0 million non-refundable up-front payment to the Company. Under the terms of the IO License and Collaboration Agreement, the parties are co-developing and co-commercializing Libtayo (cemiplimab). The parties share equally, on an ongoing basis, agreed-upon development and commercialization expenses for Libtayo. Pursuant to the Letter Agreement, the Libtayo development budget was increased and the Company allowed Sanofi to satisfy in whole or in part its funding obligations with respect to the Libtayo development and Dupilumab/Itepekimab Eligible Investments incurred in periods through September 30, 2020 by selling certain shares of our Common Stock owned by Sanofi; if Sanofi desired to sell such shares, we were able to elect to purchase, in whole or in part, such shares from Sanofi. See Note 11 for additional information regarding shares purchased by us from Sanofi.

The Company has principal control over the development of Libtayo and leads commercialization activities in the United States (see Note 2 for related product sales information), while Sanofi leads commercialization activities outside of the United States. Sanofi co-commercializes Libtayo in the United States. Each party has the right to co-commercialize licensed products in countries where it is not the lead commercialization party. The parties share equally in profits and losses in connection with the commercialization of Libtayo. In addition, the Company will be entitled to a milestone payment of $375.0 million in the event that global sales of Libtayo equal or exceed $2.0 billion in any consecutive twelve-month period.

In 2018, we and Sanofi entered into a license agreement with Bristol-Myers Squibb Company, E. R. Squibb & Sons, L.L.C., and Ono Pharmaceutical Co., Ltd. to obtain a license under certain patents owned and/or exclusively licensed by one or more of those parties that includes the right to develop and sell Libtayo. Under the agreement, we and Sanofi made an up-front payment of $20.0 million and are obligated to pay royalties of 8.0% on worldwide sales of Libtayo through December 31, 2023, and royalties of 2.5% from January 1, 2024 through December 31, 2026. The up-front payment was shared, and the royalties are shared, equally by us and Sanofi.

At the inception of the IO Collaboration, the Company's significant promised goods and services consisted of a license to certain rights and intellectual property and providing research and development services, including the manufacturing of clinical supplies. The Company concluded that the license was not distinct, primarily as a result of (i) Sanofi being unable to benefit on its own or together with other resources that are readily available as the license provides access to Regeneron's complex and specialized know-how and (ii) the research and development services, including manufacturing in support of such services, were expected to significantly modify the initial license. Therefore, the promised goods and services were considered a combined unit of account. Consequently, the $640.0 million in aggregate up-front payments made by Sanofi during 2015 in connection with the execution of the IO Collaboration was recorded within other liabilities and has been included in the transaction price.

During 2021, we updated our estimate of the total research and development costs expected to be incurred (which resulted in a change to the estimate of the stage of completion) in connection with the IO Collaboration, and, as a result, recorded a cumulative catch-up adjustment of $66.9 million as a reduction to other operating income. During 2020, we updated our estimate of the total research and development costs expected to be incurred (which resulted in a change to the estimate of the stage of completion) in connection with the Sanofi IO Collaboration, and, as a result, recorded a cumulative catch-up adjustment of $135.4 million as an increase to other operating income.

The following table summarizes contract balances in connection with the Company's IO Collaboration with Sanofi:

	As of December 31,	
(In millions)	**2021**	**2020**
Accounts receivable, net	$ (22.5)	$ (6.5)
Deferred revenue	$ 16.0	$ 10.7
Other liabilities	$ 276.1	$ 280.9

Other liabilities include up-front payments received from Sanofi for which recognition has been deferred.

The aggregate amount of the estimated consideration under the IO Collaboration related to the Company's obligation that was unsatisfied (or partially unsatisfied) as of December 31, 2021 was $570.3 million. This amount is expected to be recognized over the remaining period in which the Company is obligated to satisfy its obligation in connection with performing development activities.

b. Bayer

The Company is party to a license and collaboration agreement with Bayer for the global development and commercialization of EYLEA and aflibercept 8 mg outside the United States. All agreed-upon development expenses incurred by the Company and Bayer are shared equally. The Company is also obligated to use commercially reasonable efforts to supply clinical and commercial bulk product.

Bayer markets EYLEA outside the United States, where, for countries other than Japan, the companies share equally in profits and losses from sales. In Japan, the Company was entitled to receive a tiered percentage of between 33.5% and 40.0% of EYLEA net product sales through 2021, and thereafter, the companies share equally in profits and losses from sales. Within the United States, the Company is responsible for commercialization and retains profits from such sales. The Company is obligated to reimburse Bayer out of its share of the collaboration profits (including the Company's percentage of sales in Japan) for 50% of the agreed upon development expenses that Bayer has incurred in accordance with a formula based on the amount of development expenses that Bayer has incurred and the Company's share of the collaboration profits, or at a faster rate at the Company's option. The Company's contingent reimbursement obligation to Bayer was approximately $282 million as of December 31, 2021.

Amounts recognized in our Statements of Operations in connection with our Bayer collaboration are as follows:

(In millions)	Statement of Operations Classification	Year Ended December 31, 2021	2020	2019
Regeneron's net profit in connection with commercialization of EYLEA outside the United States	Other collaboration revenue	$ 1,349.2	$ 1,107.9	$ 1,091.4
Reimbursement for manufacturing of commercial supplies	Other collaboration revenue	$ 60.1	$ 78.2	$ 54.2
Reimbursement of development expenses	Reduction of Research and development expense	$ 46.1	$ 46.7	$ 23.0
Regeneron's obligation for its share of Bayer research and development expenses	Research and development expense	$ (40.9)	$ (35.8)	$ (20.1)

The following table summarizes contract balances in connection with our Bayer collaboration:

(In millions)	As of December 31, 2021	2020
Accounts receivable, net	$ 355.5	$ 336.2
Deferred revenue	$ 129.4	$ 99.7

c. Teva

The Company and Teva are parties to a collaboration agreement (the "Teva Collaboration Agreement") to develop and commercialize fasinumab globally, excluding certain Asian countries that are subject to our collaboration agreement with Mitsubishi Tanabe Pharma Corporation. In connection with the agreement, Teva made a $250.0 million non-refundable up-front payment in 2016. The Company leads global development activities, and the parties share development costs equally, on an ongoing basis, under a global development plan. The Company is also responsible for the manufacture and supply of fasinumab globally.

Within the United States, the Company will lead commercialization activities, and the parties will share equally in any profits and losses in connection with commercialization of fasinumab. In the territory outside the United States, Teva will lead commercialization activities and the Company will supply product to Teva at a tiered purchase price, which is calculated as a percentage of net sales of the product (subject to adjustment in certain circumstances).

As of December 31, 2021, the Company had received an aggregate $120.0 million of development milestones from Teva. The Company is entitled to receive up to an aggregate of $340.0 million in additional development milestones and up to an aggregate of $1.890 billion in contingent payments upon achievement of specified annual net sales amounts.

At the inception of the Teva Collaboration Agreement, the Company's significant promised goods and services consisted of a license to certain rights and intellectual property and providing research and development services, including the manufacturing of clinical supplies. The Company concluded that the license was not distinct, primarily as a result of (i) Teva being unable to benefit from the license on its own or together with other resources that are readily available as the license provides access to Regeneron's complex and specialized know-how and (ii) the research and development services, including manufacturing in support of such services, were expected to significantly modify the initial license. Therefore, the promised goods and services were considered a combined unit of account. Consequently, the $250.0 million up-front payment and development milestones received from Teva, as described above, have been recorded within other liabilities and included in the transaction price.

Amounts recognized in our Statements of Operations in connection with the Teva Collaboration Agreement are as follows:

(In millions)	Statement of Operations Classification	Year Ended December 31, 2021	2020	2019
Reimbursement of research and development expenses	Reduction of Research and development expense	$ 42.4	$ 109.4	$ 122.9
Amounts recognized in connection with up-front and development milestone payments received	Other operating income	$ 26.2	$ 47.2	$ 82.2

During 2020, we updated our estimate of the total research and development costs expected to be incurred (which resulted in a change to the estimate of the stage of completion) in connection with the Teva Collaboration Agreement, and, as a result, recognized a cumulative catch-up adjustment of $25.6 million as a reduction to other operating income.

The following table summarizes contract balances in connection with the Teva Collaboration Agreement:

	As of December 31,	
(In millions)	**2021**	**2020**
Accounts receivable, net	$ 11.0	$ 27.7
Other liabilities	$ 39.7	$ 66.8

Other liabilities include up-front and development milestone payments received from Teva for which recognition has been deferred.

The aggregate amount of the estimated consideration under the Teva Collaboration Agreement related to the Company's obligation that was unsatisfied (or partially unsatisfied) as of December 31, 2021 was $87.4 million. This amount is expected to be recognized over the remaining period in which the Company is obligated to satisfy its obligation in connection with performing development activities.

d. Intellia

In 2016, we entered into a license and collaboration agreement with Intellia Therapeutics, Inc. to advance CRISPR/Cas9 gene-editing technology for *in vivo* therapeutic development. The parties collaborate to conduct research for the discovery, development, and commercialization of new therapies, in addition to the research and technology development of the CRISPR/Cas9 platform.

Under the terms of the 2016 agreement, the parties agreed to a target selection process, whereby the Company may obtain exclusive rights in up to 10 targets to be chosen by the Company during the collaboration term, subject to various adjustments and limitations set forth in the agreement. Certain targets that either we or Intellia select pursuant to the target selection process may be subject to a co-development and co-commercialization arrangement at our option or Intellia's option, as applicable.

In 2020, we expanded our existing collaboration with Intellia to provide us with rights to develop products for additional *in vivo* CRISPR/Cas9-based therapeutic targets and for the parties to jointly develop potential products for the treatment of hemophilia A and B. In addition, we also received non-exclusive rights to independently develop and commercialize *ex vivo* gene edited products. In connection with the agreement, we made a $70.0 million up-front payment and purchased shares of Intellia common stock for an aggregate purchase price of $30.0 million. The up-front payment and the amount paid in excess of the fair market value of the shares purchased, or $15.0 million, were recorded to Research and development expense during 2020.

e. U.S. Government

REGEN-COV (casirivimab and imdevimab)

In the first quarter of 2020, we announced an expansion of our Other Transaction Agreement with the Biomedical Advanced Research Development Authority ("BARDA"), pursuant to which the U.S. Department of Health and Human Services ("HHS") was obligated to fund certain of our costs incurred for research and development activities related to COVID-19 treatments.

In July 2020, we entered into an agreement with entities acting at the direction of BARDA and the U.S. Department of Defense to manufacture and deliver filled and finished drug product of REGEN-COV to the U.S. government. The agreement, as subsequently amended, provided for payments to the Company of up to $465.9 million in the aggregate for bulk manufacturing of the drug substance, as well as fill/finish, storage, and other activities.

In January 2021, the Company announced an agreement with an entity acting on behalf of the U.S. Department of Defense and HHS to manufacture and deliver additional filled and finished drug product of REGEN-COV to the U.S. government. Pursuant to the agreement, the U.S. government was obligated to purchase 1.25 million doses of drug product, which we delivered by June 30, 2021, resulting in payments to the Company of $2.625 billion.

In September 2021, the Company announced an amendment to its January 2021 agreement to supply the U.S. government with an additional 1.4 million doses of REGEN-COV. Pursuant to the agreement, the U.S. government was obligated to purchase all filled and finished doses of such additional drug product delivered by January 31, 2022, resulting in payments to the Company of $2.940 billion in the aggregate. Roche supplied a portion of the doses to Regeneron to fulfill our agreement with the U.S. government (see "Roche" below for further details regarding our collaboration agreement with Roche).

As of December 31, 2021, the Company had completed its final deliveries of drug product under the agreements described above. See Note 2 for REGEN-COV net product sales recognized in connection with these agreements.

f. Roche

In August 2020, we entered into a collaboration agreement (the "Roche Collaboration Agreement") with Roche to develop, manufacture, and distribute the casirivimab and imdevimab antibody cocktail (known as REGEN-COV in the United States and Ronapreve™ in other countries). We lead global development activities for casirivimab and imdevimab, and the parties jointly fund certain ongoing studies, as well as any mutually agreed additional new global studies to evaluate further the potential of casirivimab and imdevimab in treating or preventing COVID-19.

Under the terms of the agreement, each party is obligated to dedicate a certain amount of manufacturing capacity to casirivimab and imdevimab each year. We distribute the product in the United States and Roche distributes the product outside of the United States. The parties share gross profits from worldwide sales based on a pre-specified formula, depending on the amount of manufactured product supplied by each party to the market. Each quarter, a single payment is due from one party to the other to true-up the global gross profits between the parties. If Regeneron is to receive a true-up payment from Roche, such amount will be recorded to Other collaboration revenue. If Regeneron is to make a true-up payment to Roche, such amount will be recorded to Cost of goods sold.

Amounts recognized in our Statements of Operations in connection with the Roche Collaboration Agreement are as follows:

(In millions)	Statement of Operations Classification	Year Ended December 31, 2021	Year Ended December 31, 2020
Global gross profit true-up payment from Roche in connection with sales of casirivimab and imdevimab	Other collaboration revenue	$ 361.8	—
Reimbursement of research and development expenses	Reduction of Research and development expense	$ 128.1	$ 78.5
Global gross profit true-up payment to Roche in connection with sales of casirivimab and imdevimab	Cost of goods sold	$ 259.6	—

The following table summarizes contract balances in connection with the Roche Collaboration Agreement:

(In millions)	As of December 31, 2021	As of December 31, 2020
Accounts receivable, net	—	$ 77.1
Accrued expenses and other current liabilities	$ 268.8	—

g. Alnylam

In 2019, the Company and Alnylam Pharmaceuticals, Inc. entered into a global, strategic collaboration to discover, develop, and commercialize RNA interference ("RNAi") therapeutics for a broad range of diseases by addressing therapeutic disease targets expressed in the eye and central nervous system ("CNS"), in addition to a select number of targets expressed in the liver. Under the terms of the agreement, we made an up-front payment of $400.0 million to Alnylam, which was recorded in Research and development expense during 2019. For each program, we provide Alnylam with a specified amount of funding at program initiation and at lead candidate designation, and Alnylam is eligible to receive up to an aggregate of $200.0 million in clinical proof-of-principle milestones for eye and CNS programs.

Under the collaboration, the parties plan to perform discovery research until designation of lead candidates. Following designation of a lead candidate, the parties may further advance such lead candidate under either a License Agreement or a Co-Commercialization Collaboration Agreement structure. The initial target nomination and discovery period is five years (which may under certain situations automatically be extended for up to seven years in the aggregate) (the "Research Term"). In addition, we have an option to extend the Research Term for an additional five-year period for a research extension fee ranging from $200.0 million to $400.0 million; the actual amount of the fee will be determined based on the acceptance of one or more INDs (or their equivalent in certain other countries) for programs in the eye and CNS.

In connection with the collaboration, we also purchased shares of Alnylam common stock for aggregate cash consideration of $400.0 million.

In addition, during 2019, the parties entered into a Co-Commercialization Collaboration Agreement for a silencing RNA ("siRNA") therapeutic targeting the C5 component of the human complement pathway being developed by Alnylam, with Alnylam as the lead party, and a License Agreement for a combination product consisting of such siRNA therapeutic (cemdisiran) and a fully human monoclonal antibody targeting C5 being developed by us (pozelimab), with us as the licensee. Under the C5 siRNA Co-Commercialization Collaboration Agreement, the parties share costs equally and will split profits (if commercialized); and under the License Agreement, the licensee is responsible for its own costs and expenses. The C5 siRNA License Agreement contains a flat low double-digit royalty payable to Alnylam on our potential future net sales of the combination product only subject to customary reductions, as well as up to $325.0 million in sales milestones.

h. Other

In addition to the collaboration agreements discussed above, the Company has various other collaboration agreements that are not individually significant to its operating results or financial condition at this time. Pursuant to the terms of those agreements, the Company may be required to pay, or it may receive, additional amounts contingent upon the occurrence of various future events (e.g., upon the achievement of various development and commercial milestones) which in the aggregate could be significant. The Company may also incur, or get reimbursed for, significant research and development costs if the related product candidate(s) were to advance to late stage clinical trials. In addition, if any products related to these collaborations are approved for sale, the Company may be required to pay, or it may receive, royalties on future sales. The payment or receipt of these amounts, however, is contingent upon the occurrence of various future events.

4. Marketable Securities

Marketable securities as of December 31, 2021 and 2020 consist of both available-for-sale debt securities of investment grade issuers (see below and Note 5) as well as equity securities of publicly traded companies (see Note 5).

The following tables summarize the Company's investments in available-for-sale debt securities:

(In millions)	Amortized	Unrealized		Fair
As of December 31, 2021	**Cost Basis**	**Gains**	**Losses**	**Value**
Corporate bonds	$ 7,518.4	$ 10.2	$ (40.9)	$ 7,487.7
U.S. government and government agency obligations	109.0	0.3	(0.8)	108.5
Sovereign bonds	64.4	0.3	(0.3)	64.4
Commercial paper	439.7	—	(0.1)	439.6
Certificates of deposit	255.2	—	(0.1)	255.1
Asset-backed securities	42.0	—	(0.1)	41.9
	$ 8,428.7	$ 10.8	$ (42.3)	$ 8,397.2
As of December 31, 2020				
Corporate bonds	$ 3,053.0	$ 37.5	$ (0.2)	$ 3,090.3
U.S. government and government agency obligations	127.6	1.3	—	128.9
Sovereign bonds	65.2	1.1	—	66.3
Commercial paper	276.0	0.1	—	276.1
Certificates of deposit	127.4	0.1	—	127.5
	$ 3,649.2	$ 40.1	$ (0.2)	$ 3,689.1

The Company classifies its investments in available-for-sale debt securities based on their contractual maturity dates. The available-for-sale debt securities listed as of December 31, 2021 mature at various dates through November 2026. The fair values of available-for-sale debt securities by contractual maturity consist of the following:

	As of December 31,	
(In millions)	**2021**	**2020**
Maturities within one year	$ 2,809.1	$ 1,393.3
Maturities after one year through five years	5,588.1	2,295.8
	$ 8,397.2	$ 3,689.1

The following table shows the fair value of the Company's available-for-sale debt securities that have unrealized losses, aggregated by investment category and length of time that the individual securities have been in a continuous loss position.

(In millions)	Less than 12 Months		12 Months or Greater		Total	
As of December 31, 2021	**Fair Value**	**Unrealized Loss**	**Fair Value**	**Unrealized Loss**	**Fair Value**	**Unrealized Loss**
Corporate bonds	$ 5,889.3	$ (40.9)	—	—	$ 5,889.3	$ (40.9)
U.S. government and government agency obligations	90.0	(0.8)	—	—	90.0	(0.8)
Sovereign bonds	37.0	(0.3)	—	—	37.0	(0.3)
Commercial paper	295.7	(0.1)	—	—	295.7	(0.1)
Certificates of deposit	169.4	(0.1)	—	—	169.4	(0.1)
Asset-backed securities	34.9	(0.1)	—	—	34.9	(0.1)
	$ 6,516.3	$ (42.3)	—	—	$ 6,516.3	$ (42.3)
As of December 31, 2020						
Corporate bonds	$ 364.5	$ (0.2)	—	—	$ 364.5	$ (0.2)

Realized gains and losses on sales of marketable securities were not material for the year ended December 31, 2021. Realized gains on sales of marketable securities were $29.0 million and realized losses were not material for the year ended December 31, 2020. Realized gains on sales of marketable securities were not material and there were no realized losses for the year ended December 31, 2019.

With respect to marketable securities, for the years ended December 31, 2021, 2020, and 2019, amounts reclassified from Accumulated other comprehensive income (loss) into Other income (expense), net were related to realized gains and losses on sales of available-for-sale debt securities.

5. Fair Value Measurements

The table below summarizes the Company's assets which are measured at fair value on a recurring basis. The following fair value hierarchy is used to classify assets, based on inputs to valuation techniques utilized to measure fair value:

- Level 1 - Quoted prices in active markets for identical assets
- Level 2 - Significant other observable inputs, such as quoted market prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model-based valuations in which significant inputs used are observable
- Level 3 - Significant other unobservable inputs

(In millions)		Fair Value Measurements at Reporting Date	
As of December 31, 2021	**Fair Value**	**Level 1**	**Level 2**
Available-for-sale debt securities:			
Corporate bonds	$ 7,487.7	—	$ 7,487.7
U.S. government and government agency obligations	108.5	—	108.5
Sovereign bonds	64.4	—	64.4
Commercial paper	439.6	—	439.6
Certificates of deposit	255.1	—	255.1
Asset-backed securities	41.9	—	41.9
Equity securities (unrestricted)	58.4	$ 58.4	—
Equity securities (restricted)	1,191.5	1,191.5	—
	$ 9,647.1	$ 1,249.9	$ 8,397.2
As of December 31, 2020			
Available-for-sale debt securities:			
Corporate bonds	$ 3,090.3	—	$ 3,090.3
U.S. government and government agency obligations	128.9	—	128.9
Sovereign bonds	66.3	—	66.3
Commercial paper	276.1	—	276.1
Certificates of deposit	127.5	—	127.5
Equity securities (unrestricted)	48.3	$ 48.3	—
Equity securities (restricted)	791.5	791.5	—
	$ 4,528.9	$ 839.8	$ 3,689.1

The Company held certain restricted equity securities as of December 31, 2021 which are subject to transfer restrictions that expire at various dates through 2024.

During the years ended December 31, 2021, 2020, and 2019, we recorded $386.1 million, $196.0 million, and $118.3 million of net unrealized gains, respectively, on equity securities in Other income (expense), net.

In addition to the investments summarized in the table above, as of December 31, 2021 and 2020, the Company had $40.0 million and $59.2 million, respectively, in equity investments that do not have a readily determinable fair value. These investments are recorded within Other noncurrent assets.

The fair value of our long-term debt (see Note 9), which was determined based on Level 2 inputs, was estimated to be $1.887 billion and $1.958 billion as of December 31, 2021 and 2020, respectively.

6. Inventories

Inventories consist of the following:

	As of December 31,	
(In millions)	**2021**	**2020**
Raw materials	$ 721.9	$ 459.4
Work-in-process	707.2	904.6
Finished goods	73.7	121.7
Deferred costs	448.5	430.9
	$ 1,951.3	$ 1,916.6

Inventory balances in the table above are net of reserves of $510.0 million and $136.4 million as of December 31, 2021 and 2020, respectively. Deferred costs represent the costs of product manufactured and shipped to the Company's collaborators for which recognition of revenue has been deferred. For the years ended December 31, 2021, 2020, and 2019, Cost of goods sold included inventory write-offs and reserves totaling $457.1 million, $39.2 million, and $73.8 million, respectively. Included in the 2021 write-off and reserve amount was a fourth quarter charge of $231.7 million to write down our REGEN-COV inventory as a result of data that showed REGEN-COV was highly unlikely to be active against the Omicron variant and the FDA revision of the EUA for REGEN-COV, pursuant to which REGEN-COV was no longer authorized for use in any U.S. states, territories, or jurisdictions.

7. Property, Plant, and Equipment

Property, plant, and equipment consists of the following:

	As of December 31,	
(In millions)	**2021**	**2020**
Land	$ 248.0	$ 241.2
Building and improvements	2,088.5	1,891.1
Leasehold improvements	113.9	100.5
Construction in progress	767.7	724.5
Laboratory equipment	1,225.5	1,038.6
Computer equipment and software	291.5	226.3
Furniture, office equipment, and other	145.2	130.5
	4,880.3	4,352.7
Less, accumulated depreciation and amortization	(1,398.1)	(1,131.1)
	$ 3,482.2	$ 3,221.6

Property, plant, and equipment in the table above includes leased property under the Company's finance lease at its Tarrytown, New York facility. See Note 10.

Depreciation and amortization expense on property, plant, and equipment was $281.1 million, $230.8 million, and $205.2 million for the years ended December 31, 2021, 2020, and 2019, respectively.

As of December 31, 2021 and 2020, $2.684 billion and $2.398 billion, respectively, of the Company's net property, plant, and equipment was located in the United States and $797.8 million and $823.8 million, respectively, was located in Europe (primarily in Ireland).

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	As of December 31,	
(In millions)	**2021**	**2020**
Accrued payroll and related costs	$ 440.7	$ 465.8
Accrued clinical expenses	295.8	283.0
Accrued sales-related costs	472.7	423.9
Income taxes payable	326.3	19.5
Amounts due to collaborators (see Note 3)	287.4	16.1
Other accrued expenses and liabilities	383.9	435.9
	$ 2,206.8	$ 1,644.2

9. Debt

Credit Facility

In December 2018, we entered into an agreement with a syndicate of lenders (the "Credit Agreement") which provides for a $750.0 million senior unsecured five-year revolving credit facility (the "Credit Facility"). The Credit Agreement includes an option for us to elect to increase the commitments under the Credit Facility and/or to enter into one or more tranches of term loans in the aggregate principal amount of up to $250.0 million, subject to the consent of the lenders providing the additional commitments or term loans, as applicable, and certain other conditions. Proceeds of the loans under the Credit Facility may be used to finance working capital needs, and for general corporate or other lawful purposes, of Regeneron and its subsidiaries. The Credit Agreement also provides a $50.0 million sublimit for letters of credit. The Credit Agreement includes an option for us to elect to extend the maturity date of the Credit Facility beyond December 2023, subject to the consent of the extending lenders and certain other conditions. Amounts borrowed under the Credit Facility may be prepaid, and the commitments under the Credit Facility may be terminated, at any time without premium or penalty. We had no borrowings outstanding under the Credit Facility as of December 31, 2021.

The Credit Agreement contains financial and operating covenants. The Company was in compliance with all covenants of the Credit Facility as of December 31, 2021.

Bridge Loan Facility

As described in Note 11, in the second quarter of 2020, we purchased shares of our Common Stock from Sanofi in connection with Sanofi's secondary offering of our Common Stock held by Sanofi. This purchase was partially funded with proceeds from loans under a $1.5 billion senior unsecured bridge loan facility (the "Bridge Facility") which was entered into in May 2020. The loans under the Bridge Facility bore interest at a variable interest rate based on either the London Interbank Offered Rate or the alternate base rate, plus an applicable margin that varied with our debt rating and total leverage ratio. The Bridge Facility was repaid in full during the third quarter of 2020 following the closing of the issuance and sale of the Company's senior notes (as described below).

Senior Notes

In August 2020, we issued and sold $1.250 billion aggregate principal amount of senior unsecured notes due 2030 and $750 million aggregate principal amount of senior unsecured notes due 2050 (collectively, the "Notes"). Net proceeds from the issuance and sale of the Notes (after deducting underwriting discounts and offering expenses) were used in part to repay in full the Bridge Facility described above. The underwriting discounts and offering expenses are being amortized as additional interest expense over the period from issuance through maturity.

Long-term debt in connection with our senior unsecured notes, net of underwriting discounts and offering expenses, consists of the following:

(In millions)	December 31, 2021	December 31, 2020
1.750% Senior Notes due September 2030	$ 1,239.9	$ 1,238.7
2.800% Senior Notes due September 2050	740.1	739.8
	$ 1,980.0	$ 1,978.5

Interest on each series of Notes is payable semi-annually in arrears on March 15 and September 15 of each year until their respective maturity dates. Interest expense related to the Notes was $44.4 million and $17.6 million for the years ended December 31, 2021 and 2020, respectively.

The Notes may be redeemed at the Company's option at any time at 100% of the principal amount plus accrued and unpaid interest, and, until a specified period before maturity, a specified make-whole amount. The Notes contain a change-of-control provision that, under certain circumstances, may require the Company to offer to repurchase the Notes at a price equal to 101% of the principal amount plus accrued and unpaid interest. The Notes also contain certain limitations on the Company's ability to incur liens and enter into sale and leaseback transactions, as well as customary events of default.

10. Commitments and Contingencies

See Note 15 for disclosures related to legal contingencies.

a. Leases

We conduct certain of our research, development, and administrative activities at leased facilities. We also lease certain warehouses and vehicles.

Operating leases

Amounts recognized in our Consolidated Balance Sheets and Statements of Operations included in this report associated with operating leases were not material. Operating lease right-of-use assets are included within Other noncurrent assets, and lease liabilities are included in Accrued expenses and other current liabilities and Other noncurrent liabilities.

Finance leases

In March 2017, we entered into a Participation Agreement with BA Leasing BSC, LLC, an affiliate of Banc of America Leasing & Capital LLC ("BAL"), as lessor, and a syndicate of lenders (collectively with BAL, the "Lease Participants"), which provided for $720.0 million of lease financing from the Lease Participants for the acquisition of laboratory and office facilities in Tarrytown, New York (the "Facility"). In March 2017, we also entered into a Lease and Remedies Agreement with BAL, pursuant to which we have leased the Facility from BAL for a five-year term ending in March 2022. The Participation Agreement, the Lease and Remedies Agreement, and certain other related agreements were amended and restated in May 2019, among other things, to revise certain covenants, representations and warranties, and events of default to be substantially similar to those set forth in our Credit Facility (as so amended and restated, the "Participation Agreement" and the "Lease," respectively). The Lease requires us to pay all maintenance, insurance, taxes, and other costs arising out of the use of the Facility. We are also required to make monthly payments of basic rent during the term of the Lease in an amount equal to a variable rate per annum based on the one-month LIBOR, plus an applicable margin that varies with our debt rating and total leverage ratio. The Participation Agreement and the Lease include an option for us to elect to extend the maturity date of the Participation Agreement and the term of the Lease for an additional five-year period, subject to the consent of all the Lease Participants and certain other conditions. We also have the option prior to the end of the term of the Lease to (a) purchase the Facility by paying an amount equal to the outstanding principal amount of the Lease Participants' advances under the Participation Agreement, all accrued and unpaid interest and yield thereon, and all other outstanding amounts under the Participation Agreement, the Lease, and certain related documents or (b) sell the Facility to a third party on behalf of BAL. The advances under the Participation Agreement mature, and all amounts outstanding thereunder will become due and payable in full, at the end of the term of the Lease.

In September 2021, we delivered a request to the Lease Participants to potentially exercise the option for a five-year extension of the term of the Lease and the maturity date under the Participation Agreement. In November 2021, the Lease Participants consented to such extension, subject to the satisfaction of certain conditions prior to the expiration of the existing term in March 2022, including the negotiation and execution of satisfactory definitive documentation setting forth the terms and conditions that would apply during such potential extended term. We are negotiating such documentation with the Lease Participants, but there can be no assurance that such extension will become effective.

The Lease is classified as a finance lease as we have the option to purchase the Facility under terms that make it reasonably certain to be exercised. The agreements governing the Lease financing contain financial and operating covenants. The Company was in compliance with all such covenants as of December 31, 2021.

Amounts recognized in the Consolidated Balance Sheet related to the Lease are included in the table below. Other than the Lease described above, we had no leases accounted for as finance leases as of December 31, 2021 and 2020.

		As of December 31,	
(In millions)	**Classification**	**2021**	**2020**
Finance lease right-of-use assets	Property, plant, and equipment, net[1]	$ 631.3	$ 645.7
Finance lease liabilities	Finance lease liabilities	$ 719.7	$ 717.2

[1] Finance lease right-of-use assets were recorded net of accumulated amortization of $104.9 million and $90.5 million as of December 31, 2021 and 2020, respectively.

Finance lease costs consist of the following:

	Year Ended December 31,	
(In millions)	**2021**	**2020**
Amortization of right-of-use assets	$ 14.4	$ 14.4
Interest on lease liabilities	11.9	15.7
	$ 26.3	$ 30.1

Other information related to our finance lease includes the following:

	As of December 31,	
	2021	**2020**
Remaining lease term (in years)	0.2	1.2
Discount rate	1.68%	1.66%

Supplemental information

The following is a maturity analysis of our finance lease liabilities:

(In millions)	**As of December 31, 2021**
2022	$ 723.0
2023	—
2024	—
2025	—
2026	—
Thereafter	—
Total undiscounted lease payments	723.0
Imputed interest	(2.9)
Debt financing costs	(0.4)
Total lease liabilities	$ 719.7

b. Research Collaboration and Licensing Agreements

As part of our research and development efforts, we enter into research collaboration and licensing agreements with other companies, universities, and other organizations. These agreements contain varying terms and provisions which include fees to be paid by the Company, services to be provided, and license rights to certain proprietary technology developed under the agreements. Some of these agreements may require the Company to pay additional amounts contingent upon the occurrence of various future events (e.g., upon the achievement of various development and commercial milestones). Additionally, we have in-licensed patent and/or technology pursuant to agreements which contain provisions that require the Company to pay royalties, as defined, at rates that range from 0.5% to 10.0%, in the event the Company sells or licenses any proprietary products developed under the respective agreements. The Company also has contingent reimbursement obligations to its collaborators Sanofi and Bayer out of the respective collaboration's profits, if they are sufficient for that purpose. See Note 3 for a more detailed description of collaboration, license, and other agreements.

For the years ended December 31, 2021, 2020, and 2019, the Company recorded royalty expense (net of reimbursements from collaborators, as applicable) in Cost of goods sold and Cost of collaboration and contract manufacturing of $66.9 million, $56.5 million, and $47.0 million, respectively, based on product sales of commercial products under various licensing agreements.

11. Stockholders' Equity

The Company's Restated Certificate of Incorporation, as amended, provides for the issuance of up to 40 million shares of Class A Stock, par value $0.001 per share, and 320 million shares of Common Stock, par value $0.001 per share. Shares of Class A Stock are convertible, at any time, at the option of the holder into shares of Common Stock on a share-for-share basis. Holders of Class A Stock have rights and privileges identical to Common Stockholders except that each share of Class A is entitled to ten votes per share, while each share of Common Stock is entitled to one vote per share. Class A Stock may only be transferred to specified Permitted Transferees, as defined. Under the Company's Restated Certificate of Incorporation, the Company's board of directors is authorized to issue up to 30 million shares of Preferred Stock, in series, with rights, privileges, and qualifications of each series determined by the board of directors.

Share Repurchase Programs

In November 2019, our board of directors authorized a share repurchase program to repurchase up to $1.0 billion of our Common Stock. The share repurchase program permitted the Company to make repurchases through a variety of methods, including open-market transactions (including pursuant to a trading plan adopted in accordance with Rule 10b5-1 of the Exchange Act), privately negotiated transactions, accelerated share repurchases, block trades, and other transactions in compliance with Rule 10b-18 of the Exchange Act. As of December 31, 2020, the Company had repurchased the entire $1.0 billion it was authorized to repurchase under the program.

In January 2021, our board of directors authorized a share repurchase program to repurchase up to $1.5 billion of our Common Stock. The share repurchase program was approved under terms substantially similar to the November 2019 share repurchase program described above. As of December 31, 2021, the Company had repurchased the entire $1.5 billion of its Common Stock that it was authorized to repurchase under the program.

In November 2021, our board of directors authorized an additional share repurchase program to repurchase up to $3.0 billion of our Common Stock. The share repurchase program was approved under terms substantially similar to the share repurchase programs above. Repurchases may be made from time to time at management’s discretion, and the timing and amount of any such repurchases will be determined based on share price, market conditions, legal requirements, and other relevant factors. The program has no time limit and can be discontinued at any time. There can be no assurance as to the timing or number of shares of any repurchases in the future. As of December 31, 2021, $2.845 billion remained available for share repurchases under the November 2021 program.

The table below summarizes the shares of our Common Stock we repurchased under the programs described above and the cost of the shares received, which were recorded as Treasury Stock.

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
Number of shares repurchased	3.0	1.6	0.7
Total cost of shares received	$ 1,655.0	$ 746.0	$ 254.0

Sanofi Funding of Certain Development Costs

As described in Note 3, in 2018, we and Sanofi entered into a Letter Agreement, which, among other things, granted Sanofi a limited waiver of Sanofi's lock-up obligations under the amended and restated investor agreement between us and Sanofi in order to allow Sanofi to satisfy its funding obligations with respect to Libtayo development costs and/or Dupilumab/Itepekimab Eligible Investments for quarterly periods ending on September 30, 2020 by selling our Common Stock owned by Sanofi. During 2020 and 2019, Sanofi elected to sell, and we elected to purchase, shares of our Common Stock to satisfy Sanofi's funding obligation related to such activities. Consequently, we recorded the cost of the shares received, or $135.0 million and $102.7 million, as Treasury Stock during 2020 and 2019, respectively.

Additional Stock Purchased from Sanofi

In May 2020, a secondary offering of 13,014,646 shares of our Common Stock (the "Secondary Offering") held by Sanofi was completed. In connection with the Secondary Offering, we also purchased 9,806,805 shares directly from Sanofi for an aggregate purchase amount of $5.0 billion (the "Stock Purchase"). See Note 9 for additional information. As a result of the Secondary Offering and the Stock Purchase, Sanofi disposed of all of its shares of our Common Stock, other than 400,000 shares that it retained as of the closing of the Secondary Offering and the Stock Purchase (a portion of which Sanofi used for the funding of certain development costs described above).

In May 2020, the Company entered into an amendment to the amended and restated investor agreement, which provides, among other things, that following the Secondary Offering and Share Purchase, (1) the “standstill” provisions, which contractually prohibit Sanofi from seeking to directly or indirectly exert control of the Company, continue to apply pursuant to their terms and (2) the voting commitments contained in the investor agreement continue to apply to the shares of Common Stock held by Sanofi and its affiliates following the secondary offering and stock repurchase, for so long as such shares are held by them.

Arrangements with Other Collaborators

In connection with the Company's license and collaboration agreements with Bayer for the joint development and commercialization outside the United States of antibody product candidates to PDGFR-beta and Ang2, Bayer is bound by certain "standstill" provisions, which contractually prohibit Bayer from seeking to influence the control of the Company or acquiring more than 20% of the Company's outstanding shares of Class A Stock and Common Stock (taken together). With respect to each of these agreements, this prohibition will remain in place until the earliest of (i) the fifth anniversary of the termination of the agreement (which, in the case of the PDGFR-beta license and collaboration agreement, will occur on July 31, 2022, and, in the case of the Ang2 agreement, will occur on November 1, 2023) or (ii) other specified events.

Further, pursuant to the 2016 Teva Collaboration Agreement, Teva and its affiliates are bound by certain "standstill" provisions, which contractually prohibit them from seeking to directly or indirectly exert control of the Company or acquiring more than 5% of the Company's Class A Stock and Common Stock (taken together). This prohibition will remain in place until the earliest of (i) the fifth anniversary of the expiration or earlier termination of the agreement or (ii) other specified events.

12. Long-Term Incentive Plans

The Company has used long-term incentive plans for the purpose of granting equity awards to employees of the Company, including officers, and non-employees, including non-employee members of the Company's board of directors (collectively, "Participants"). The Participants may receive awards as determined by a committee of independent members of the Company's board of directors or, to the extent authorized by such committee with respect to certain Participants, a duly authorized employee (collectively, the "Committee"). The incentive plan currently used by the Company is the Second Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (the "Second Amended and Restated 2014 Incentive Plan"). It was most recently adopted and approved by the Company's shareholders in 2020. As of the most recent shareholder approval date, the Second Amended and Restated 2014 Incentive Plan provided for the issuance of up to 22.3 million shares of Common Stock in respect of awards. In addition, upon expiration, forfeiture, surrender, exchange, cancellation, or termination of any award previously granted under the Amended and Restated Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (the "Amended and Restated 2014 Incentive Plan"), the Regeneron Pharmaceuticals, Inc. 2014 Long-Term Incentive Plan (the "Original 2014 Incentive Plan"), or the Second Amended and Restated 2000 Long-Term Incentive Plan (the "2000 Incentive Plan"), any shares subject to such award are added to the pool of shares available for grant under the Second Amended and Restated 2014 Incentive Plan.

The awards that may be made under the Second Amended and Restated 2014 Incentive Plan include: (a) incentive stock options and non-qualified stock options, (b) restricted stock awards, (c) shares of phantom stock (also referred to as restricted stock units, which may be time- or performance-based), and (d) other awards. Any award granted may (but is not required to) be subject to vesting based on the attainment by the Company of performance goals pre-established by the Committee.

Stock option awards grant Participants the right to purchase shares of Common Stock at prices determined by the Committee, with exercise prices that are equal to or greater than the average of the high and low market prices of the Company's Common Stock on the date of grant (the "Market Price"). Options vest over a period of time determined by the Committee, generally on a pro rata basis over a four-year period. The Committee also determines the expiration date of each option. The maximum term of options that have been awarded under the 2000 Incentive Plan, the Original 2014 Incentive Plan, the Amended and Restated 2014 Incentive Plan, and the Second Amended and Restated 2014 Incentive Plan (collectively, the "Incentive Plans") is ten years.

Restricted stock awards grant Participants shares of restricted Common Stock or allow Participants to purchase such shares at a price determined by the Committee. Such shares are nontransferable for a period determined by the Committee ("vesting period"). Should employment terminate, as specified in the Incentive Plans, except as determined by the Committee in its discretion and subject to the applicable Incentive Plan documents, the ownership of any unvested restricted stock awards will be transferred to the Company.

Phantom stock awards provide the Participant the right to receive Common Stock or an amount of cash based on the value of the Common Stock at a future date. The award is subject to such restrictions, if any, as the Committee may impose at the date of grant or thereafter, including a specified period of employment or the achievement of performance goals. Time-based restricted stock units and performance-based restricted stock units are each a type of phantom stock award permitted under the Second Amended and Restated 2014 Incentive Plan.

The Incentive Plans contain provisions that allow for the Committee to provide for the immediate vesting of awards upon a change in control of the Company, as defined in the Incentive Plans.

As of December 31, 2021, there were 17.9 million shares available for future grants under the Second Amended and Restated 2014 Incentive Plan. No additional awards may be made under the 2000 Incentive Plan, the Original 2014 Incentive Plan, or the Amended and Restated 2014 Incentive Plan.

a. Stock Options

Transactions involving stock option awards during 2021 under the Company's Incentive Plans are summarized in the table below.

	Number of Shares *(In millions)*	Weighted -Average Exercise Price	Weighted-Average Remaining Contractual Term *(In years)*	Intrinsic Value *(In millions)*
Outstanding as of December 31, 2020	21.7	$ 379.51		
2021: Granted	2.3	$ 628.43		
Forfeited	(0.4)	$ 419.51		
Exercised	(5.6)	$ 299.23		
Outstanding as of December 31, 2021	18.0	$ 435.56	6.5	$ 3,654.5
Vested and expected to vest as of December 31, 2021	17.2	$ 431.33	6.3	$ 3,566.6
Exercisable as of December 31, 2021	11.3	$ 398.83	5.2	$ 2,697.6

The Company satisfies stock option exercises with newly issued shares of the Company's Common Stock. The total intrinsic value of stock options exercised during 2021, 2020, and 2019 was $1.707 billion, $2.251 billion, and $558.9 million, respectively. The intrinsic value represents the amount by which the market price of the underlying stock exceeds the exercise price of an option.

The table below summarizes the weighted-average exercise prices and weighted-average grant-date fair values of options issued during the years ended December 31, 2021, 2020, and 2019.

	Number of Options Granted *(In millions)*	Weighted-Average Exercise Price	Weighted-Average Fair Value
2021:			
Exercise price equal to Market Price	2.3	$ 628.43	$ 174.20
2020:			
Exercise price equal to Market Price	2.9	$ 492.60	$ 126.50
2019:			
Exercise price equal to Market Price	3.3	$ 366.65	$ 100.80

For the years ended December 31, 2021, 2020, and 2019, the Company recognized $328.7 million, $329.5 million, and $422.8 million, respectively, of non-cash stock-based compensation expense related to stock option awards (net of amounts capitalized as inventory, which were not material for each of the three years). As of December 31, 2021, there was $515.9 million of stock-based compensation cost related to unvested stock options, net of estimated forfeitures, which had not yet been recognized. The Company expects to recognize this compensation cost over a weighted-average period of 1.8 years.

Fair Value Assumptions:

The following table summarizes the weighted average values of the assumptions used in computing the fair value of option grants during 2021, 2020, and 2019.

	2021	2020	2019
Expected volatility	27 %	28 %	28 %
Expected lives from grant date	5.5 years	5.0 years	5.0 years
Expected dividend yield	0 %	0 %	0 %
Risk-free interest rate	1.22 %	0.47 %	1.74 %

Expected volatility has been estimated based on actual movements in the Company's stock price over the most recent historical periods equivalent to the options' expected lives. Expected lives are principally based on the Company's historical exercise experience with previously issued employee and board of directors' option grants. The expected dividend yield is zero as the Company has never paid dividends and does not currently anticipate paying any in the foreseeable future. The risk-free interest rates are based on quoted U.S. Treasury rates for securities with maturities approximating the options' expected lives.

b. Restricted Stock Awards and Time-Based Restricted Stock Units

A summary of the Company's activity related to restricted stock awards and time-based restricted stock units (excluding performance-based restricted stock units, which are detailed further below) (collectively, "restricted stock") during 2021 is summarized below.

	Number of Shares/Units *(In millions)*	Weighted-Average Grant Date Fair Value
Balance as of December 31, 2020	1.7	$ 421.58
2021: Granted	0.7	$ 633.31
Vested	(0.2)	$ 374.17
Forfeited	(0.1)	$ 440.08
Balance as of December 31, 2021	2.1	$ 499.85

The Company recognized non-cash stock-based compensation expense related to restricted stock of $221.0 million, $102.5 million, and $29.7 million in 2021, 2020, and 2019, respectively (net of amounts capitalized as inventory, which were not material for each of the three years). As of December 31, 2021, there was $649.1 million of stock-based compensation cost related to unvested restricted stock which had not yet been recognized. The Company expects to recognize this compensation cost over a weighted-average period of 2.4 years.

c. Performance-based Restricted Stock Units

Performance-based restricted stock units ("PSUs") have been granted to certain executive officers of the Company. The PSUs will be earned based upon the achievement of predetermined, cumulative total shareholder return goals with respect to the Company's Common Stock price over a specified (generally five-year) period beginning on the grant date. The number of PSUs granted represents the maximum number of units that are eligible to be earned. Depending on the terms of the PSUs and the outcome of the performance goals, a recipient may ultimately earn 0% to 250% (as specified for each PSU grant) of the target number of PSUs granted. As of December 31, 2021 and 2020, 1.3 million PSUs were outstanding with a weighted-average grant date fair value of $209.06 per unit. During the year ended December 31, 2021, the Company did not grant new PSUs and no PSUs were vested, forfeited, or cancelled.

The Company recognized non-cash stock-based compensation expense related to PSUs of $52.0 million and $11.7 million in 2021 and 2019, respectively. The Company did not recognize non-cash stock-based compensation expense related to PSUs in 2020 (as PSUs granted in 2020 were granted on December 31, 2020 and are expensed over the vesting period). As of December 31, 2021, there was $208.0 million of stock-based compensation cost related to unvested PSUs which had not yet been recognized. The Company expects to recognize this compensation cost on a straight-line basis over a period of 4.0 years.

Fair Value Assumptions:

The following table summarizes the weighted average values of the assumptions used in computing the fair value of PSUs that were granted during 2020 and 2019.

	2020	2019
Expected volatility	35%	33%
Expected dividend yield	0%	0%
Risk-free interest rate	0.36%	1.63%

13. Employee Savings Plans

The Company maintains the Regeneron Pharmaceuticals, Inc. 401(k) Savings Plan, as amended and restated (the "Savings Plan"). The terms of the Savings Plan allow U.S. employees (as defined by the Savings Plan) to contribute to the Savings Plan a percentage of their compensation. In addition, the Company may make discretionary contributions, as defined, to the accounts of participants under the Savings Plan. The Company also maintains additional employee savings plans outside of the United States, which cover eligible employees.

Expenses recognized by the Company related to contributions to such plans were not material during 2021, 2020, and 2019.

14. Income Taxes

The Company is subject to U.S. federal, state, and foreign income taxes. Components of income before income taxes consist of the following:

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
United States	$ 5,944.7	$ 2,442.3	$ 2,011.2
Foreign	3,381.1	1,368.1	417.9
	$ 9,325.8	$ 3,810.4	$ 2,429.1

Components of income tax expense consist of the following:

	Year Ended December 31,		
(In millions)	**2021**	**2020**	**2019**
Current:			
Federal	$ 1,429.8	$ 199.0	$ 444.6
State	6.2	1.2	1.9
Foreign	(38.4)	21.4	(2.6)
Total current tax expense	1,397.6	221.6	443.9
Deferred:			
Federal	(423.2)	109.0	(132.0)
State	(0.6)	(2.0)	(1.7)
Foreign	276.7	(31.4)	3.1
Total deferred tax (benefit) expense	(147.1)	75.6	(130.6)
	$ 1,250.5	$ 297.2	$ 313.3

A reconciliation of the U.S. statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2021	**2020**	**2019**
U.S. federal statutory tax rate	21.0 %	21.0 %	21.0 %
Taxation of non-U.S. operations	(2.8)	(1.8)	(1.0)
Stock-based compensation	(2.4)	(7.6)	(2.5)
Foreign-derived intangible income deduction	(1.4)	—	(1.6)
Income tax credits	(1.0)	(2.8)	(4.6)
Sale of non-inventory related assets between foreign subsidiaries	—	(0.8)	—
Other permanent differences	—	(0.2)	1.6
Effective income tax rate	13.4 %	7.8 %	12.9 %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities are as follows:

	As of December 31,	
(In millions)	**2021**	**2020**
Deferred tax assets:		
Deferred compensation	$ 406.6	$ 436.6
Accrued expenses	262.1	139.8
Fixed assets and intangible assets	257.5	140.5
Deferred revenue	57.3	44.6
Other	16.9	14.9
Total deferred tax assets	1,000.4	776.4
Deferred tax liabilities:		
Unrealized gains on investments	(123.5)	(57.7)
Net deferred tax assets	$ 876.9	$ 718.7

The Company's federal income tax returns for 2017 through 2020 remain open to examination by the IRS. The Company's 2017 and 2018 federal income tax returns are currently under audit by the IRS. In general, the Company's state income tax returns from 2016 to 2020 remain open to examination. The Company's income tax returns outside of the United States remain open to examination from 2018 to 2020. The United States and many states generally have statutes of limitation ranging from 3 to 5 years; however, those statutes could be extended due to the Company's tax credit carryforward position. In general, tax authorities have the ability to review income tax returns in which the statute of limitation has previously expired to adjust the tax credits generated in those years.

The following table reconciles the beginning and ending amounts of unrecognized tax benefits. The amount of unrecognized tax benefits that, if settled, would impact the effective tax rate is $410.9 million, $267.0 million, and $210.8 million as of December 31, 2021, 2020, and 2019, respectively.

(In millions)	**2021**	**2020**	**2019**
Balance as of January 1	$ 267.0	$ 210.8	$ 189.5
Gross increases related to current year tax positions	182.3	76.6	37.9
Gross increases (decreases) related to prior year tax positions	2.9	7.2	(7.2)
Gross decreases due to settlements and lapse of statutes of limitations	(41.3)	(27.6)	(9.4)
Balance as of December 31	$ 410.9	$ 267.0	$ 210.8

During 2021, the decreases in unrecognized tax benefits related to the Company's federal income tax returns for 2015 and 2016, as these audits are closed. In 2021, 2020, and 2019, the increases in unrecognized tax benefits primarily related to the Company's calculation of certain tax credits and other items related to the Company's international operations.

During 2021, 2020, and 2019, interest expense related to unrecognized tax benefits recorded by the Company was not material. The Company does not believe that it is reasonably possible that the resolution of tax exposures within the next twelve months would have a material impact on its unrecognized tax benefits as of December 31, 2021.

15. Legal Matters

From time to time, the Company is a party to legal proceedings in the course of the Company's business. Costs associated with the Company's involvement in legal proceedings are expensed as incurred. The outcome of any such proceedings, regardless of the merits, is inherently uncertain. The Company recognizes accruals for loss contingencies associated with such proceedings when it is probable that a liability will be incurred and the amount of loss can be reasonably estimated. As of December 31, 2021 and 2020, the Company's accruals for loss contingencies were not material. If the Company were unable to prevail in any such proceedings, its consolidated financial position, results of operations, and future cash flows may be materially impacted.

Proceedings Relating to Praluent (alirocumab) Injection

As described in greater detail below, the Company is currently a party to patent infringement actions initiated by Amgen Inc. (and/or its affiliated entities) against the Company and/or Sanofi (and/or the Company's and Sanofi's respective affiliated entities) in a number of jurisdictions relating to Praluent. See Note 3 for a description of the Company's and Sanofi's arrangement regarding the costs resulting from or associated with such actions.

United States

In the United States, Amgen has asserted claims of U.S. Patent Nos. 8,829,165 (the "'165 Patent") and 8,859,741 (the "'741 Patent"), and sought a permanent injunction to prevent the Company and the Sanofi defendants from commercial manufacturing, using, offering to sell, or selling within the United States (as well as importing into the United States) (collectively, "Commercializing") Praluent. Amgen also seeks a judgment of patent infringement of the asserted patents, monetary damages (together with interest), costs and expenses of the lawsuits, and attorneys' fees. As described in greater detail under "Second Jury Trial and Appeal" below, on February 11, 2021, the Federal Circuit (as defined below) affirmed the lower court's decision that certain of Amgen's asserted patent claims are invalid based on lack of enablement.

First Jury Trial and Appeal. The first jury trial in this litigation (the "First Trial") was held in the United States District Court for the District of Delaware (the "District Court") from March 8 to March 16, 2016. During the course of the First Trial, the District Court ruled as a matter of law in favor of Amgen that the asserted patent claims were not obvious, and in favor of the Company and the Sanofi defendants that there was no willful infringement of the asserted patent claims by the Company or the Sanofi defendants. On March 16, 2016, the jury returned a verdict in favor of Amgen in the First Trial, finding that the asserted claims of the '165 and '741 Patents were not invalid based on either a lack of written description or a lack of enablement. On October 5, 2017, the United States Court of Appeals for the Federal Circuit (the "Federal Circuit") reversed in part the District Court's decision and remanded for a new trial on the issues of written description and enablement. In addition, it affirmed the District Court's ruling that Amgen's patents were not obvious.

Second Jury Trial and Appeal. On January 3, 2019, the District Court held oral argument in the remanded proceedings on the Company and the Sanofi defendants' motion for judgment on the pleadings regarding Amgen's willful infringement claim. On January 18, 2019, the District Court entered an order (i) denying the Company and the Sanofi defendants' motion for summary judgment on validity, (ii) denying Amgen's motion for partial summary judgment on estoppel, and (iii) granting the Company and the Sanofi defendants' cross-motion for summary judgment on estoppel. On February 8, 2019, the District Court granted the Company and the Sanofi defendants' motion for judgment on the pleadings, thereby dismissing Amgen's claim of willful infringement. The second jury trial in this litigation (the "Second Trial") was held before the District Court in February 2019 to determine the validity of Amgen's asserted patent claims. On February 25, 2019, the jury returned a verdict in the Second Trial generally in favor of Amgen, finding that two claims of the '165 Patent and one claim of the '741 Patent were not invalid. The jury also found that two claims of the '165 Patent were invalid for lack of adequate written description while rejecting the lack of enablement challenges to those two claims. On August 28, 2019, the District Court ruled as a matter of law that Amgen's asserted patent claims are invalid based on lack of enablement. The District Court also conditionally denied the Company and the Sanofi defendants' motion for a new trial. On October 23, 2019, Amgen filed a notice of appeal of the District Court's decision with the Federal Circuit. An oral hearing before the Federal Circuit was held on December 9, 2020. On February 11, 2021, the Federal Circuit affirmed the District Court's decision that certain of Amgen's asserted patent claims are invalid based on lack of enablement. On April 14, 2021, Amgen filed a petition for a rehearing en banc, which was denied on June 21, 2021. On November 18, 2021, Amgen filed a petition for writ of certiorari with the United States Supreme Court.

Injunctive Relief Proceedings. On March 18, 2019, Amgen filed a renewed motion for a permanent injunction to prohibit the Company and the Sanofi defendants from Commercializing Praluent in the United States (a "Permanent Injunction"), and an oral hearing on this motion was held in June 2019. Previously, the Federal Circuit stayed and then vacated a Permanent Injunction granted by the District Court in connection with the First Trial. On August 28, 2019, the District Court dismissed as moot Amgen's renewed motion for a Permanent Injunction.

Europe

Amgen has asserted European Patent No. 2,215,124 (the "'124 Patent"), which pertains to PCSK9 monoclonal antibodies, in the countries in Europe discussed below. In October 2020, the '124 Patent claims directed to compositions of matter and medical use relevant to Praluent were ruled invalid based on a lack of inventive step by the Technical Board of Appeal (the "TBA") of the European Patent Office (the "EPO"). This decision impacted each of the infringement proceedings based on the '124 Patent discussed below.

Amgen filed lawsuits in Germany, the United Kingdom, and France in July 2016, July 2016, and September 2016, respectively, against the Company and certain of Sanofi's affiliated entities for infringement of the relevant designation of the '124 Patent in each such jurisdiction; and these lawsuits were dismissed in November 2020, September 2021, and June 2021, respectively. The dismissal in Germany followed an earlier finding of infringement and granting of an injunction, both of which were subsequently overturned. In December 2019, Amgen also filed lawsuits in the Netherlands, Italy, and Spain for infringement of the relevant designation of the '124 Patent in each such jurisdiction; the Company was not named as a defendant in any of these actions, and each of these lawsuits was dismissed in February 2021.

Japan

As previously reported, on March 31, 2020, Amgen filed a lawsuit in the Tokyo District Court against Sanofi K.K. seeking damages incurred by Amgen as a result of the earlier finding of infringement of Amgen's Japanese Patent Nos. 5,906,333 and 5,705,288 by the Tokyo District Court Civil Division. The Company has not been named as a defendant in this damages action.

Proceedings Relating to Dupixent (dupilumab) Injection

United States

On March 23, 2017, the Company, Sanofi-Aventis U.S. LLC, and Genzyme Corporation initiated an *inter partes* review ("IPR") in the United States Patent and Trademark Office ("USPTO") seeking a declaration of invalidity of U.S. Patent No. 8,679,487 (the "'487 Patent") owned by Immunex Corporation relating to antibodies that bind the human interleukin-4 receptor and subsequently filed two additional IPR petitions in the USPTO seeking declarations of invalidity of the '487 Patent based on different grounds (the "Additional IPR Petitions"). The Patent Trial and Appeal Board ("PTAB") of the USPTO issued a final written decision on the Additional IPR Petitions on February 14, 2019, invalidating all 17 claims of the '487 Patent as obvious. This decision was subsequently affirmed by the Federal Circuit and Immunex's petition for writ of certiorari was denied by the United States Supreme Court. The '487 Patent expired in May 2020 following Immunex's filing of a terminal disclaimer with the USPTO.

On April 5, 2017, Immunex Corporation filed a lawsuit against the Company, Sanofi, Sanofi-Aventis U.S. LLC, Genzyme Corporation, and Aventisub LLC in the United States District Court for the Central District of California seeking a judgment of patent infringement of the '487 Patent and a declaratory judgment of infringement of the '487 Patent, in each case by the Company's and the other defendants' Commercializing of Dupixent; monetary damages (together with interest); an order of willful infringement of the '487 Patent, which would allow the court in its discretion to award damages up to three times the amount assessed; costs and expenses of the lawsuit; and attorneys' fees. The court subsequently granted a joint stipulation by the parties to stay the litigation pending resolution of the appeals of the PTAB's final written decisions on the Additional IPR Petitions discussed above; and, on August 3, 2021, granted a motion to dismiss the lawsuit, dismissing all of Immunex's claims with prejudice.

Europe

On September 30, 2016, Sanofi initiated a revocation proceeding in the United Kingdom to invalidate the U.K. counterpart of European Patent No. 2,292,665 (the "'665 Patent"), another patent owned by Immunex relating to antibodies that bind the human interleukin-4 receptor. At the joint request of the parties to the revocation proceeding, the U.K. Patents Court ordered on January 30, 2017 that the revocation action be stayed pending the final determination of the currently pending EPO opposition proceedings initiated by the Company and Sanofi in relation to the '665 Patent. The oral hearing before the EPO on the oppositions occurred on November 20, 2017, at which the claims of the '665 Patent were found invalid and the patent was revoked. A final written decision of revocation of the '665 Patent was issued by the EPO on January 4, 2018. Immunex filed a notice of appeal of the EPO's decision on January 31, 2018, and an oral hearing before the TBA has been scheduled for March 10–11, 2022. On September 20, 2017 and September 21, 2017, respectively, the Company and Sanofi initiated opposition proceedings in the EPO against Immunex's European Patent No. 2,990,420 (the "'420 Patent"), a divisional patent of the '665 Patent (i.e., a patent that shares the same priority date, disclosure, and patent term of the parent '665 Patent but contains claims to a different invention). The oral hearing before the EPO on the oppositions occurred on February 14–15, 2019, at which the '420 Patent was revoked in its entirety. Immunex filed a notice of appeal of the EPO's decision on May 31, 2019, and an oral hearing before the TBA has been scheduled for March 10–11, 2022. The original patent term of the Immunex patents expired in May 2021.

Proceedings Relating to EYLEA (aflibercept) Injection

On January 7, 2021, Chengdu Kanghong Pharmaceutical Group Co., Ltd. ("Chengdu Kanghong") filed an IPR petition in the USPTO against the Company' s U.S. Patent No. 10,464,992 (the "'992 Patent") and a post-grant review ("PGR") petition against the Company's U.S. Patent No. 10,828,345 (the "'345 Patent") seeking declarations of invalidity of the '992 Patent and '345 Patent. On June 23, 2021, Chengdu Kanghong filed motions to dismiss each of these petitions and terminate the respective proceedings, which were granted by the USPTO on June 25, 2021.

On February 11, 2020, anonymous parties filed two requests for *ex parte* reexamination of the Company's U.S. Patent No. 10,406,226 and the '992 Patent, and the USPTO has granted both requests to initiate reexamination proceedings.

On May 5, 2021, Mylan Pharmaceuticals Inc. filed IPR petitions in the USPTO against the Company's U.S. Patent Nos. 9,254,338 (the "'338 Patent") and 9,669,069 (the "'069 Patent") seeking declarations of invalidity of the '338 Patent and the '069 Patent. On November 10, 2021, the USPTO issued a decision instituting both IPR proceedings. On December 9, 2021, Apotex Inc. and Celltrion, Inc. each filed two separate IPR petitions against the Company's '338 and '069 Patents requesting that their IPRs be instituted and joined with the IPR proceedings initiated by Mylan concerning the '338 and '069 Patents.

On September 7, 2021, Celltrion, Inc. filed a PGR petition in the USPTO against the Company's U.S. Patent No. 10,857,231 (the "'231 Patent") seeking a declaration of invalidity of the '231 Patent.

On October 26 and October 27, 2021, anonymous parties initiated opposition proceedings in the EPO against the Company's European Patent No. 2,944,306 (the "'306 Patent") seeking revocation of the '306 Patent in its entirety.

Proceedings Relating to EYLEA (aflibercept) Injection Pre-filled Syringe

On June 19, 2020, Novartis Pharma AG, Novartis Pharmaceuticals Corporation, and Novartis Technology LLC (collectively, "Novartis") filed a complaint with the U.S. International Trade Commission (the "ITC") pursuant to Section 337 of the Tariff Act of 1930 requesting that the ITC institute an investigation relating to the importation into the United States and/or sale within the United States after importation of EYLEA pre-filled syringes ("PFS") and/or components thereof which allegedly infringe Novartis's U.S. Patent No. 9,220,631 (the "'631 Patent"). Novartis also requested a permanent limited exclusion order forbidding entry into the United States of EYLEA PFS or components thereof; a permanent cease-and-desist order from the importation, sale, offer for sale, advertising, packaging, or solicitation of any sale by the Company of EYLEA PFS or components thereof; and a bond should the Company continue to import EYLEA PFS (if found to infringe) during, if applicable, any 60-day Presidential review period (i.e., the period when the President of the United States (or his designee) can disapprove any ITC decision to issue an exclusion order or cease-and-desist order). The ITC instituted the investigation on July 22, 2020 and a trial was scheduled for April 19–23, 2021. On March 26, 2021, the staff attorney appointed by the ITC's Office of Unfair Import Investigations ("OUII") —an independent government party to the case representing the public interest—determined that the '631 Patent is invalid on several grounds. On April 8, 2021, Novartis moved to terminate the ITC investigation in its entirety based on its withdrawal of the complaint; and, on May 3, 2021, the ITC terminated the investigation.

On June 19, 2020, Novartis also filed a patent infringement lawsuit (as amended on August 2, 2021) in the U.S. District Court for the Northern District of New York asserting claims of the '631 Patent and seeking preliminary and permanent injunctions to prevent the Company from continuing to infringe the '631 Patent. Novartis also seeks a judgment of patent infringement of the '631 Patent, monetary damages (together with interest), an order of willful infringement of the '631 Patent (which would allow the court in its discretion to award damages up to three times the amount assessed), costs and expenses of the lawsuits, and attorneys' fees. On July 30, 2020, the court granted the Company's motion to stay these proceedings until a determination in the ITC proceedings discussed above, including any appeals therefrom, becomes final. On June 11, 2021, the court, at the request of Novartis, lifted the stay. On November 5, 2021, the Company filed a motion to stay these proceedings in light of the pending IPR proceeding discussed below. On January 31, 2022, the court denied the Company's motion to stay these proceedings.

On July 16, 2020, the Company initiated two IPR petitions in the USPTO seeking a declaration of invalidity of the '631 Patent on two separate grounds. On January 15, 2021, the USPTO declined to institute an IPR proceeding on procedural grounds in light of the pending ITC investigation discussed above; the other IPR petition has been withdrawn. Following Novartis's motion to terminate the ITC investigation discussed above, on April 16, 2021 the Company filed a new IPR petition seeking a declaration of invalidity of the '631 Patent based on the same grounds that were the basis for the OUII staff attorney's determination discussed above. On October 26, 2021, the USPTO issued a decision instituting the IPR proceeding.

On July 17, 2020, the Company filed an antitrust lawsuit against Novartis and Vetter Pharma International Gmbh ("Vetter") in the United States District Court for the Southern District of New York seeking a declaration that the '631 Patent is unenforceable and a judgment that the defendants' conduct violates Sections 1 and 2 of the Sherman Antitrust Act of 1890, as amended (the "Sherman Antitrust Act"). The Company is also seeking injunctive relief and treble damages. On September 4, 2020, Novartis filed, and Vetter moved to join, a motion to dismiss the complaint, to transfer the lawsuit to the Northern District of New York, or to stay the suit; and on October 19, 2020, Novartis filed, and Vetter moved to join, a second motion to dismiss the complaint on different grounds. On January 25, 2021, the Company filed an amended complaint seeking a judgment that Novartis's conduct violates Section 2 of the Sherman Antitrust Act based on additional grounds, as well as a judgment of tortious interference with contract. On February 22, 2021, Novartis filed, and Vetter moved to join, a motion to dismiss the amended complaint. On September 21, 2021, the court granted Novartis and Vetter's motion to transfer this lawsuit to the Northern District of New York. As a result, this lawsuit was transferred to the same judge that had been assigned to the patent infringement lawsuit discussed above. On November 5, 2021, the Company filed a motion to stay these proceedings in light of the pending IPR proceeding

discussed above. On January 31, 2022, the court denied the Company's motion to stay these proceedings and granted Novartis and Vetter's motion to dismiss the amended complaint.

Proceedings Related to "Most Favored Nation" Interim Final Rule

On December 11, 2020, the Company filed a lawsuit in the United States District Court for the Southern District of New York against the U.S. Department of Health and Human Services, the Secretary of HHS, the Centers for Medicare & Medicaid Services ("CMS"), and the Administrator of CMS seeking declaratory and injunctive relief related to the interim final rule with comment period entitled "Most Favored Nation (MFN) Model" issued on November 20, 2020 by HHS, acting through CMS (the "MFN Rule"). On the same day, the Company filed a motion for a preliminary injunction and temporary restraining order, seeking to prevent implementation of the MFN Rule. On December 22, 2020, the court heard oral argument on the Company's motion for a preliminary injunction and temporary restraining order. On December 31, 2020, the court granted the Company's motion and issued a preliminary injunction. On February 2, 2021, the government stated to the court that the Solicitor General had determined not to appeal the preliminary injunction. On February 10, 2021, the court entered a 90-day stay of the litigation and subsequently extended the stay, with the most recent 60-day extension granted on January 4, 2022. On December 27, 2021, CMS published a final rule that rescinds the MFN Rule effective February 28, 2022.

Proceedings Relating to fasinumab

On May 21, 2020, the Company and Teva Pharmaceutical Industries Limited ("Teva") filed a lawsuit against Rinat Neurosciences Corp. ("Rinat"), a wholly owned subsidiary of Pfizer Inc., in the English High Court of Justice in London, seeking invalidation and revocation of Rinat's European Patent No. 2,270,048 (the "'048 Patent"), European Patent No. 1,871,416 (the "'416 Patent"), and European Patent No. 2,305,711 (the "'711 Patent"), each of which pertains to the use of NGF monoclonal antibodies to treat certain symptoms in patients suffering from osteoarthritis. On July 21, 2020, Rinat filed its defense and counterclaim seeking a declaration of infringement of the '048 Patent by fasinumab. The counterclaim also seeks a permanent injunction, damages, an accounting of profits, and costs and interest. On December 15, 2020, Rinat filed an amended defense and counterclaim seeking a declaration of infringement of the '711 Patent by fasinumab. On May 5, 2021, the court stayed this litigation on terms mutually agreed by the parties.

The '048 Patent is subject to opposition proceedings in the EPO, which were initiated by the Company on August 10, 2016 and two other opponents on August 11, 2016. On January 3, 2018, the Opposition Division of the EPO issued a preliminary, non-binding opinion regarding the validity of the '048 Patent, indicating that it considered the granted patent to be invalid. An oral hearing on the oppositions against the '048 Patent was held on November 29–30, 2018, at which the Opposition Division upheld the validity of the '048 Patent's claims in amended form. The Company filed a notice of appeal to the TBA of the EPO on March 7, 2019. On October 21, 2020, Teva filed a notice of intervention with the TBA to take part in the appeal proceedings as an intervener. An oral hearing before the TBA has been scheduled for April 5–6, 2022.

The '711 Patent is also subject to opposition proceedings in the EPO, which were initiated by the Company on May 1, 2018. On January 31, 2019, the Opposition Division of the EPO issued a preliminary, non-binding opinion regarding the validity of the '711 Patent, indicating that it considered the granted patent to be invalid. An oral hearing on the opposition against the '711 Patent was held on December 3, 2019, at which the Opposition Division upheld the validity of the '711 Patent's claims in amended form. The Company filed a notice of appeal to the TBA on December 20, 2019. On January 29, 2021, Teva filed a notice of intervention with the TBA to take part in the appeal proceedings as an intervener. An oral hearing before the TBA was held on July 29, 2021, at which the '711 Patent was revoked in its entirety.

Proceedings Relating to REGEN-COV (casirivimab and imdevimab)

On October 5, 2020, Allele Biotechnology and Pharmaceuticals, Inc. ("Allele") filed a lawsuit (as amended on April 8, 2021) against the Company in the United States District Court for the Southern District of New York, asserting infringement of U.S. Patent No. 10,221,221 (the "'221 Patent"). Allele seeks a judgment of patent infringement of the '221 Patent, an award of monetary damages (together with interest), an order of willful infringement of the '221 Patent (which would allow the court in its discretion to award damages up to three times the amount assessed), costs and expenses of the lawsuit, and attorneys' fees. On July 16, 2021, the Company filed a motion to dismiss the complaint. An oral hearing has been scheduled for March 2, 2022.

Department of Justice Matters

In January 2017, the Company received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents relating to its support of 501(c)(3) organizations that provide financial assistance to patients; documents concerning its provision of financial assistance to patients with respect to products sold or developed by Regeneron (including EYLEA, Praluent, ARCALYST, and ZALTRAP®); and certain other related documents and communications. On June 24, 2020, the U.S. Attorney's Office for the District of Massachusetts filed a civil complaint in the U.S. District Court for the District of Massachusetts alleging violations of the federal Anti-Kickback Statute, and asserting causes of action under the federal False Claims Act and state law. On August 24, 2020, the Company filed a motion to dismiss the complaint in its entirety. On December 4, 2020, the court denied the motion to dismiss.

In September 2019, the Company and Regeneron Healthcare Solutions, Inc., a wholly-owned subsidiary of the Company, each received a civil investigative demand ("CID") from the U.S. Department of Justice pursuant to the federal False Claims Act relating to remuneration paid to physicians in the form of consulting fees, advisory boards, speaker fees, and payment or reimbursement for travel and entertainment allegedly in violation of the federal Anti-Kickback Statute. The CIDs relate to EYLEA, Praluent, Dupixent, ZALTRAP, ARCALYST, and Kevzara and cover the period from January 2015 to the present. On June 3, 2021, the United States District Court for the Central District of California unsealed a *qui tam* complaint filed against the Company, Regeneron Healthcare Solutions, Inc., and Sanofi-Aventis U.S. LLC by two *qui tam* plaintiffs (known as relators) purportedly on behalf the United States and various states (the "State Plaintiffs"), asserting causes of action under the federal False Claims Act and state law. Also on June 3, 2021, the United States and the State Plaintiffs notified the court of their decision to decline to intervene in the case. On October 29, 2021, the *qui tam* plaintiffs filed an amended complaint in this matter. On January 14, 2022, the Company filed a motion to dismiss the amended complaint in its entirety.

In June 2021, the Company received a CID from the U.S. Department of Justice pursuant to the federal False Claims Act. The CID states that the investigation concerns allegations that the Company (i) violated the False Claims Act by paying kickbacks to distributors and ophthalmology practices to induce purchase of EYLEA, including through discounts, rebates, credit card fees, free units of EYLEA, and inventory management systems; and (ii) inflated reimbursement rates for EYLEA by excluding applicable discounts, rebates, and benefits from the average sales price reported to CMS. The CID covers the period from January 2011 through June 2021. The Company is cooperating with this investigation.

Proceedings Initiated by UnitedHealthcare

On December 17, 2020, UnitedHealthcare Insurance Company and United Healthcare Services, Inc. (collectively, "UHC") filed a lawsuit against the Company in the United States District Court for the Southern District of New York alleging UHC has been damaged by the conduct alleged in the civil complaint filed by the U.S. Attorney's Office for the District of Massachusetts discussed under "Department of Justice Matters" above. UHC alleges causes of action under state law and the federal Racketeer Influenced and Corrupt Organizations Act (the "RICO Act") and seeks monetary damages and equitable relief. On March 1, 2021, the Company filed a motion to dismiss the complaint in its entirety. On March 25, 2021, UHC filed an amended complaint; and, on April 22, 2021, the Company filed a motion to dismiss this amended complaint in its entirety. On December 29, 2021, this lawsuit was stayed pending resolution of the proceedings before the U.S. District Court for the District of Massachusetts discussed under "Department of Justice Matters" above.

Proceedings Initiated by Humana

On July 22, 2021, Humana Inc. ("Humana") filed a lawsuit against the Company in the United States District Court for the Southern District of New York alleging Humana has been damaged by the conduct alleged in the civil complaint filed by the U.S. Attorney's Office for the District of Massachusetts discussed under "Department of Justice Matters" above. Humana alleges causes of action under state law and the RICO Act and seeks monetary damages and equitable relief. On September 27, 2021, the Company filed a motion to dismiss the complaint in its entirety. On December 29, 2021, this lawsuit was stayed pending resolution of the proceedings before the U.S. District Court for the District of Massachusetts discussed under "Department of Justice Matters" above.

Proceedings Initiated by Blue Cross and Blue Shield

On December 20, 2021, Blue Cross and Blue Shield of Massachusetts, Inc. and Blue Cross and Blue Shield of Massachusetts HMO Blue, Inc. (collectively, "BCBS") filed a lawsuit against the Company in the U.S. District Court for the District of Massachusetts alleging BCBS has been damaged by the conduct alleged in the civil complaint filed by the U.S. Attorney's Office for the District of Massachusetts discussed under "Department of Justice Matters" above. BCBS alleges causes of action under state law and the RICO Act and seeks monetary damages and equitable relief.

Shareholder Demand

On or about September 30, 2020, the Company's board of directors received a demand letter from a purported shareholder of the Company. The demand alleges that Regeneron and its shareholders have been damaged by the conduct alleged in the civil complaint filed by the U.S. Attorney's Office for the District of Massachusetts discussed under "Department of Justice Matters" above. The demand letter requests that the Company's board of directors investigate alleged breaches of fiduciary duty by its officers and directors and other alleged violations of law and corporate governance practices and procedures; bring legal action against the persons responsible for causing the alleged damages; and implement and maintain an effective system of internal controls, compliance mechanisms, and corporate governance practices and procedures. The Company's board of directors, working with outside counsel, investigated and evaluated the allegations in the demand letter and has concluded that pursuing the claims alleged in the demand would not be in the Company's best interests at this time.

Proceedings Relating to Shareholder Derivative Complaint

On June 29, 2021, an alleged shareholder filed a shareholder derivative complaint in the New York Supreme Court, naming the current and certain former members of the Company's board of directors and certain current and former executive officers of the Company as defendants and Regeneron as a nominal defendant. The complaint asserts that the individual defendants breached their fiduciary duties in relation to the allegations in the civil complaint filed by the U.S. Attorney's Office for the District of Massachusetts discussed under "Department of Justice Matters" above. The complaint seeks an award of damages allegedly sustained by the Company; an order requiring Regeneron to take all necessary actions to reform and improve its corporate governance and internal procedures; disgorgement from the individual defendants of all profits and benefits obtained by them resulting from their sales of Regeneron stock; and costs and disbursements of the action, including attorneys' fees. On July 28, 2021, the defendants filed a notice of removal, removing the case from the New York Supreme Court to the U.S. District Court for the Southern District of New York. On September 24, 2021, the individual defendants moved to dismiss the complaint in its entirety. Also on September 24, 2021, the plaintiff filed a motion to remand the case to the New York Supreme Court.

16. Net Income Per Share

The calculations of basic and diluted net income per share are as follows:

	Year Ended December 31,		
(In millions, except per share data)	**2021**	**2020**	**2019**
Net income - basic and diluted	$ 8,075.3	$ 3,513.2	$ 2,115.8
Weighted average shares - basic	105.7	107.6	109.2
Effect of dilutive securities:			
Stock options	5.4	7.0	5.4
Restricted stock awards and restricted stock units	1.1	0.5	—
Weighted average shares - diluted	112.2	115.1	114.6
Net income per share - basic	$ 76.40	$ 32.65	$ 19.38
Net income per share - diluted	$ 71.97	$ 30.52	$ 18.46

Shares which have been excluded from diluted per share amounts because their effect would have been antidilutive include the following:

	Year Ended December 31,		
(Shares in millions)	**2021**	**2020**	**2019**
Stock options	2.9	2.7	18.4

17. Statement of Cash Flows

The following provides a reconciliation of cash, cash equivalents, and restricted cash reported within the Consolidated Balance Sheet to the total of the same such amounts shown in the Consolidated Statement of Cash Flows:

	December 31,		
(In millions)	**2021**	**2020**	**2019**
Cash and cash equivalents	$ 2,885.6	$ 2,193.7	$ 1,617.8
Restricted cash included in Other noncurrent assets	12.5	13.6	12.5
Total cash, cash equivalents, and restricted cash shown in the Consolidated Statement of Cash Flows	$ 2,898.1	$ 2,207.3	$ 1,630.3

Restricted cash consists of amounts held by financial institutions pursuant to contractual arrangements.

Supplemental disclosure of non-cash investing and financing activities

Included in accounts payable, accrued expenses, and other liabilities as of December 31, 2021, 2020, and 2019 were $74.8 million, $83.6 million, and $133.7 million, respectively, of accrued capital expenditures.

DIRECTORS

P. Roy Vagelos, M.D. (Chair)
Former President, Chief Executive Officer, and Chair of the Board of Merck & Co., Inc.

Bonnie L. Bassler, Ph.D.
Chair of the Department of Molecular Biology and Squibb Professor in Molecular Biology at Princeton University

Michael S. Brown, M.D
Distinguished Chair in Biomedical Sciences and Regental Professor of Molecular Genetics and Internal Medicine and Director of the Jonsson Center for Molecular Genetics at The University of Texas Southwestern Medical Center at Dallas

N. Anthony Coles, M.D.
President and Chief Executive Officer and Chair of the Board of Cerevel Therapeutics Holdings, Inc., the parent entity of Cerevel Therapeutics, Inc.

Joseph L. Goldstein, M.D.
Professor of Molecular Genetics and Internal Medicine and the Chair of the Department of Molecular Genetics at The University of Texas Southwestern Medical Center at Dallas

Christine A. Poon
Former Vice Chair and Worldwide Chair of Pharmaceuticals at Johnson & Johnson

Arthur F. Ryan
Former Chief Executive Officer and Chair of the Board of Prudential Financial, Inc.

Leonard S. Schleifer, M.D., Ph.D.
President and Chief Executive Officer of Regeneron Pharmaceuticals, Inc.

George L. Sing
Chief Executive Officer of GanD, Inc. and Chair of Grace Science, LLC

Marc Tessier-Lavigne, Ph.D.
President of Stanford University

George D. Yancopoulos, M.D., Ph.D.
President and Chief Scientific Officer of Regeneron Pharmaceuticals, Inc.

Huda Y. Zoghbi, M.D.
Professor in the Departments of Pediatrics, Molecular and Human Genetics, and Neurology and Neuroscience at Baylor College of Medicine

EXECUTIVE OFFICERS

Leonard S. Schleifer, M.D., Ph.D.
President and Chief Executive Officer

George D. Yancopoulos, M.D., Ph.D.
President and Chief Scientific Officer

Christopher Fenimore
Senior Vice President, Controller

Robert E. Landry
Executive Vice President, Finance and Chief Financial Officer

Joseph J. LaRosa
Executive Vice President, General Counsel and Secretary

Marion McCourt
Executive Vice President, Commercial

Andrew J. Murphy, Ph.D.
Executive Vice President, Research

Neil Stahl, Ph.D.
Executive Vice President, Research and Development

Daniel P. Van Plew
Executive Vice President and General Manager, Industrial Operations and Product Supply

CORPORATE INFORMATION

COMMON STOCK AND RELATED MATTERS

Our Common Stock is traded on The NASDAQ Global Select Market under the symbol “REGN.” Our Class A Stock is not publicly quoted or traded.

SHAREHOLDERS’ INQUIRIES

Inquiries relating to stock transfer or lost certificates and notices of changes of address should be directed to our Transfer Agent, American Stock Transfer & Trust Co., 6201 15th Avenue, Brooklyn, New York 11219, (800) 937-5449, www.amstock.com/main. General information regarding the Company, recent press releases, and filings with the U.S. Securities and Exchange Commission are available on our website at www.regeneron.com, or can be obtained by contacting our Investor Relations Department at (914) 847-7741 or invest@regeneron.com.

TRANSFER AGENT & REGISTRAR

American Stock Transfer & Trust Co.
6201 15th Avenue
Brooklyn, New York 11219

CORPORATE OFFICE

777 Old Saw Mill River Road
Tarrytown, New York 10591-6707
(914) 847-7000

ANNUAL MEETING

The 2022 Annual Meeting of Shareholders will be held virtually via the Internet at www.virtualshareholdermeeting.com/REGN2022 on June 10, 2022 at 10:30 a.m., Eastern Time.

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

PricewaterhouseCoopers LLP

REGENERON

SCIENCE TO MEDICINE®