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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended October 1, 2021

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number: 000-30235

EXELIXIS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3257395**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

1851 Harbor Bay Parkway
Alameda, CA 94502
(650) 837-7000

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock $.001 Par Value per Share	**EXEL**	**The Nasdaq Stock Market LLC**

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 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 Securities Act. ☐

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

As of October 25, 2021, there were 316,397,360 shares of the registrant's common stock outstanding.

EXELIXIS, INC.
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PART I - FINANCIAL INFORMATION

Item 1. Financial Statements

EXELIXIS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except per share amounts)
(unaudited)

	September 30, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 567,325	$ 319,217
Short-term investments	835,406	887,319
Trade receivables, net	179,493	160,875
Inventory	28,240	20,973
Prepaid expenses and other current assets	51,564	57,011
Total current assets	1,662,028	1,445,395
Long-term investments	362,218	330,751
Property and equipment, net	99,838	67,384
Deferred tax assets, net	125,295	156,711
Goodwill	63,684	63,684
Other long-term assets	134,678	73,408
Total assets	$ 2,447,741	$ 2,137,333
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 24,314	$ 23,632
Accrued compensation and benefits	53,306	51,189
Accrued clinical trial liabilities	70,618	52,251
Rebates and fees due to customers	31,120	20,683
Accrued collaboration liabilities	35,403	12,456
Other current liabilities	54,747	44,447
Total current liabilities	269,508	204,658
Long-term portion of deferred revenues	9,444	3,755
Long-term portion of operating lease liabilities	52,252	49,086
Other long-term liabilities	4,090	721
Total liabilities	335,294	258,220
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000 shares authorized and no shares issued	—	—
Common stock, $0.001 par value; 400,000 shares authorized; issued and outstanding: 316,305 and 311,627 at September 30, 2021 and December 31, 2020, respectively	316	312
Additional paid-in capital	2,422,323	2,321,895
Accumulated other comprehensive income	1,481	4,476
Accumulated deficit	(311,673)	(447,570)
Total stockholders' equity	2,112,447	1,879,113
Total liabilities and stockholders' equity	$ 2,447,741	$ 2,137,333

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

EXELIXIS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF INCOME (LOSS)
(in thousands, except per share amounts)
(unaudited)

	Three Months Ended September 30, 2021	Three Months Ended September 30, 2020	Nine Months Ended September 30, 2021	Nine Months Ended September 30, 2020
Revenues:				
Net product revenues	$ 263,117	$ 168,587	$ 774,577	$ 541,197
License revenues	49,694	33,205	116,862	113,318
Collaboration services revenues	15,612	29,300	92,391	62,971
Total revenues	328,423	231,092	983,830	717,486
Operating expenses:				
Cost of goods sold	11,874	8,725	39,956	27,235
Research and development	163,370	176,762	471,448	393,572
Selling, general and administrative	101,558	88,185	302,404	210,916
Total operating expenses	276,802	273,672	813,808	631,723
Income (loss) from operations	51,621	(42,580)	170,022	85,763
Interest income	1,658	3,994	6,231	16,376
Other income (expense), net	(19)	565	(120)	571
Income (loss) before income taxes	53,260	(38,021)	176,133	102,710
Provision for (benefit from) income taxes	15,056	(5,981)	40,236	19,317
Net income (loss)	$ 38,204	$ (32,040)	$ 135,897	$ 83,393
Net income (loss) per share:				
Basic	$ 0.12	$ (0.10)	$ 0.43	$ 0.27
Diluted	$ 0.12	$ (0.10)	$ 0.42	$ 0.26
Weighted-average common shares outstanding:				
Basic	315,380	309,116	313,990	307,437
Diluted	322,022	309,116	322,084	317,495

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

EXELIXIS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands)
(unaudited)

	Three Months Ended September 30, 2021	Three Months Ended September 30, 2020	Nine Months Ended September 30, 2021	Nine Months Ended September 30, 2020
Net income (loss)	$ 38,204	$ (32,040)	$ 135,897	$ 83,393
Other comprehensive income (loss):				
Net unrealized gains (losses) on available-for-sale debt securities, net of tax impact of $193, $453, $949 and $(893), respectively	(504)	(1,601)	(2,995)	3,170
Comprehensive income (loss)	$ 37,700	$ (33,641)	$ 132,902	$ 86,563

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

EXELIXIS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(unaudited)

	Three Months Ended September 30, 2021					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at June 30, 2021	314,822	$ 315	$ 2,390,654	$ 1,985	$ (349,877)	$ 2,043,077
Net income	—	—	—	—	38,204	38,204
Other comprehensive loss	—	—	—	(504)	—	(504)
Issuance of common stock under equity incentive plans	1,483	1	3,304	—	—	3,305
Stock transactions associated with taxes withheld on equity awards	—	—	(5,958)	—	—	(5,958)
Stock-based compensation	—	—	34,323	—	—	34,323
Balance at September 30, 2021	$ 316,305	$ 316	$ 2,422,323	$ 1,481	$ (311,673)	$ 2,112,447

	Three Months Ended September 30, 2020					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at June 30, 2020	308,886	$ 309	$ 2,269,093	$ 7,840	$ (443,918)	$ 1,833,324
Net loss	—	—	—	—	(32,040)	(32,040)
Other comprehensive loss	—	—	—	(1,601)	—	(1,601)
Issuance of common stock under equity incentive plans	516	—	1,872	—	—	1,872
Stock transactions associated with taxes withheld on equity awards	—	—	(5,179)	—	—	(5,179)
Stock-based compensation	—	—	55,655	—	—	55,655
Balance at September 30, 2020	$ 309,402	$ 309	$ 2,321,441	$ 6,239	$ (475,958)	$ 1,852,031

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EXELIXIS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY - Continued
(in thousands)
(unaudited)

	Nine Months Ended September 30, 2021					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2020	311,627	$ 312	$ 2,321,895	$ 4,476	$ (447,570)	$ 1,879,113
Net income	—	—	—	—	135,897	135,897
Other comprehensive loss	—	—	—	(2,995)	—	(2,995)
Issuance of common stock under equity incentive and stock purchase plans	4,678	4	18,788	—	—	18,792
Stock transactions associated with taxes withheld on equity awards	—	—	(15,371)	—	—	(15,371)
Stock-based compensation	—	—	97,011	—	—	97,011
Balance at September 30, 2021	316,305	$ 316	$ 2,422,323	$ 1,481	$ (311,673)	$ 2,112,447

	Nine Months Ended September 30, 2020					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	304,831	$ 305	$ 2,241,947	$ 3,069	$ (559,351)	$ 1,685,970
Net income	—	—	—	—	83,393	83,393
Other comprehensive income	—	—	—	3,170	—	3,170
Issuance of common stock under equity incentive and stock purchase plans	4,571	4	19,823	—	—	19,827
Stock transactions associated with taxes withheld on equity awards	—	—	(26,120)	—	—	(26,120)
Stock-based compensation	—	—	85,791	—	—	85,791
Balance at September 30, 2020	309,402	$ 309	$ 2,321,441	$ 6,239	$ (475,958)	$ 1,852,031

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

EXELIXIS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(unaudited)

	Nine Months Ended September 30,	
	2021	2020
Net income	$ 135,897	$ 83,393
Adjustments to reconcile net income to net cash provided by operating activities:		
Depreciation	11,699	6,731
Stock-based compensation	96,654	85,791
Non-cash lease expense	3,952	3,607
Deferred taxes	32,365	15,803
Other, net	35,871	1,609
Changes in operating assets and liabilities:		
Trade receivables, net	(20,124)	(47,074)
Inventory	(26,956)	(13,466)
Prepaid expenses and other assets	(24,252)	(15,868)
Deferred revenue	11,434	4,012
Accounts payable and other liabilities	47,812	51,151
Net cash provided by operating activities	304,352	175,689
Cash flows from investing activities:		
Purchases of property, equipment and other	(48,265)	(16,055)
Purchases of investments	(1,077,377)	(866,975)
Proceeds from maturities and sales of investments	1,095,813	781,324
Net cash used in investing activities	(29,829)	(101,706)
Cash flows from financing activities:		
Proceeds from issuance of common stock under equity incentive and stock purchase plans	18,242	19,682
Taxes paid related to net share settlement of equity awards	(15,049)	(26,120)
Net cash provided by (used in) financing activities	3,193	(6,438)
Net increase in cash, cash equivalents and restricted cash equivalents	277,716	67,545
Cash, cash equivalents and restricted cash equivalents at beginning of period	320,772	268,137
Cash, cash equivalents and restricted cash equivalents at end of period	$ 598,488	$ 335,682
Supplemental cash flow disclosures:		
Non-cash operating activities:		
Right-of-use assets obtained in exchange for lease obligations	$ 4,893	$ 1,824
Non-cash investing activities:		
Unpaid liabilities incurred for purchases of property and equipment	$ 5,143	$ 843
Unpaid liabilities incurred in asset acquisition	$ 9,000	$ —

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

EXELIXIS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(unaudited)

NOTE 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Organization

Exelixis, Inc. (Exelixis, we, our or us) is an oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. We have invented and brought to market novel, effective and tolerable therapies using our drug discovery and development resources and capabilities and commercialization platform; we will continue to build on this foundation, working toward providing cancer patients with additional treatment options.

Since our founding in 1994, four products resulting from our discovery efforts have progressed through clinical development, received regulatory approval and established a commercial presence in various geographies around the world. Our flagship molecule, cabozantinib, is an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET and has been approved by the U.S. Food and Drug Administration (FDA) and foreign regulatory authorities as two products: CABOMETYX® (cabozantinib) tablets approved for advanced renal cell carcinoma (RCC), both alone and in combination with Bristol Myers Squibb Company's OPDIVO® (nivolumab), and for previously treated hepatocellular carcinoma (HCC) and, in the U.S. only, for previously treated, radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC) and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer (MTC). For these types of cancer, cabozantinib has become or is becoming a standard of care.

The other two products resulting from our discovery efforts are: COTELLIC® (cobimetinib), an inhibitor of MEK, approved as part of multiple combination regimens to treat specific forms of advanced melanoma and marketed under a collaboration with Genentech, Inc. (a member of the Roche Group) (Genentech); and MINNEBRO® (esaxerenone), an oral, non-steroidal, selective blocker of the mineralocorticoid receptor, approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo Company, Limited (Daiichi Sankyo).

Leveraging the revenue stream derived from our cabozantinib franchise and other marketed products, we are expanding our oncology product pipeline through drug discovery efforts, which encompass both small molecule and biologics programs with multiple modalities and mechanisms of action.

Basis of Presentation

The accompanying Condensed Consolidated Financial Statements include the accounts of Exelixis and those of our wholly owned subsidiaries. These entities' functional currency is the U.S. dollar. All intercompany balances and transactions have been eliminated.

The accompanying unaudited Condensed Consolidated Financial Statements have been prepared in accordance with accounting principles generally accepted in the U.S. for interim financial information and pursuant to Form 10-Q and Article 10 of Regulation S-X of the Securities and Exchange Commission (SEC). Accordingly, they do not include all of the information and footnotes required by U.S. generally accepted accounting principles for complete financial statements. In our opinion, all adjustments (consisting only of normal recurring adjustments) considered necessary for a fair presentation of our financial statements for the periods presented have been included. Operating results for the three and nine months ended September 30, 2021 are not necessarily indicative of the results that may be expected for the year ending December 31, 2021 or for any future period. The accompanying Condensed Consolidated Financial Statements and Notes thereto should be read in conjunction with our Consolidated Financial Statements and Notes thereto for the year ended December 31, 2020, included in our Annual Report on Form 10-K submitted to the SEC on February 10, 2021.

We have adopted a 52- or 53-week fiscal year policy that generally ends on the Friday closest to December 31st. Fiscal year 2021, which is a 52-week fiscal year, will end on December 31, 2021 and fiscal year 2020, which was a 52-week fiscal year, ended on January 1, 2021. For convenience, references in this report as of and for the fiscal periods ended July 2, 2021 and July 3, 2020, October 1, 2021 and October 2, 2020, and as of and for the fiscal year ended January 1, 2021, are indicated as being as of and for the fiscal periods ended June 30, 2021 and June 30, 2020, September 30, 2021 and September 30, 2020, and the year ended December 31, 2020, respectively.

Segment Information

We operate in one business segment that focuses on the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Our Chief Executive Officer, as the chief operating decision-maker, manages and allocates resources to our operations on a total consolidated basis. Consistent with this decision-making process, our Chief Executive Officer uses consolidated, single-segment financial information for purposes of evaluating performance, forecasting future period financial results, allocating resources and setting incentive targets.

All of our long-lived assets are located in the U.S. See “Note 2. Revenues” for enterprise-wide disclosures about product sales, revenues from major customers and revenues by geographic region.

Use of Estimates

The preparation of the accompanying Condensed Consolidated Financial Statements conforms to accounting principles generally accepted in the U.S., which requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosures. On an ongoing basis, we evaluate our significant estimates. We base our estimates on historical experience and on various other market-specific and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ materially from those estimates.

Reclassifications

Certain prior period amounts in the accompanying Condensed Consolidated Financial Statements have been reclassified to conform to the current period presentation. Such reclassifications did not impact previously reported total revenues, income (loss) from operations, net income (loss), total assets, total liabilities or total stockholders’ equity.

Significant Accounting Policies

Except for the foreign currency forward contracts for non-designated hedges, there have been no material changes to our significant accounting policies during the nine months ended September 30, 2021, as compared to the significant accounting policies disclosed in Note 1 – Significant Accounting Policies included in our Annual Report on Form 10-K for the year ended December 31, 2020.

Foreign Currency Forward Contracts for Non-Designated Hedges

We may use forward foreign currency exchange contracts (forward contracts) to hedge certain operational exposures resulting from potential changes in foreign currency exchange rates. Our strategy is to enter into forward contracts so that increases or decreases in our foreign currency exposures are offset by gains or losses on the foreign currency forward contracts thereby mitigating the risks and volatility associated with our foreign currency transactions. We do not apply hedge accounting treatment to these non-designated hedging instruments. We do not hold or issue derivative instruments for trading or speculative purposes.

Our forward contracts are generally short-term in duration. Given the short duration of the forward contracts, amounts recorded generally are not significant. We account for our derivative instruments as either assets or liabilities on our Condensed Consolidated Balance Sheets and measure them at fair value. Derivatives not designated as hedging instruments are adjusted to fair value through earnings in other income (expense), net in the Condensed Consolidated Statements of Income (Loss).

Recently Adopted Accounting Pronouncements

On January 1, 2021, we adopted the Accounting Standards Board’s (FASB) Accounting Standards Update (ASU) 2019-12, *Income Taxes (Topic 740)-Simplifying the Accounting for Income Taxes* (ASU 2019-12). ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in Accounting Standards Codification (ASC) Topic 740, *Income Taxes* and clarifying and amending existing guidance. Our adoption of ASU 2019-12 did not have a significant impact on the accompanying Condensed Consolidated Financial Statements.

Recent Accounting Pronouncements Not Yet Adopted

There were no new accounting pronouncements issued since our filing of the Annual Report on Form 10-K for the year ended December 31, 2020, which could have a significant effect on our condensed consolidated financial statements.

NOTE 2. REVENUES

Revenues consisted of the following (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Product revenues:				
Gross product revenues	$ 357,462	$ 220,401	$ 1,051,871	$ 702,865
Discounts and allowances	(94,345)	(51,814)	(277,294)	(161,668)
Net product revenues	263,117	168,587	774,577	541,197
Collaboration revenues:				
License revenues	49,694	33,205	116,862	113,318
Collaboration services revenues	15,612	29,300	92,391	62,971
Total collaboration revenues	65,306	62,505	209,253	176,289
Total revenues	$ 328,423	$ 231,092	$ 983,830	$ 717,486

The percentage of total revenues by customer who individually accounted for 10% or more of our total revenues were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Ipsen Pharma SAS	12 %	16 %	17 %	16 %
Affiliates of McKesson Corporation	15 %	12 %	15 %	13 %
Affiliates of CVS Health Corporation	16 %	14 %	15 %	15 %
Affiliates of AmerisourceBergen Corporation	16 %	11 %	14 %	11 %
Affiliates of Optum Specialty Pharmacy	9 %	10 %	9 %	11 %
Takeda Pharmaceutical Company Limited	7 %	10 %	3 %	7 %

The percentage of trade receivables by customer who individually accounted for 10% or more of our trade receivables were as follows:

	September 30, 2021	December 31, 2020
Ipsen Pharma SAS	24 %	23 %
Affiliates of McKesson Corporation	19 %	12 %
Affiliates of AmerisourceBergen Corporation	16 %	11 %
Affiliates of CVS Health Corporation	13 %	11 %
Takeda Pharmaceutical Company Limited	3 %	10 %

Revenues by geographic region were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
U.S.	$ 266,436	$ 171,552	$ 783,583	$ 549,379
Europe	38,095	36,006	162,822	117,959
Japan	23,892	23,534	37,425	50,148
Total revenues	$ 328,423	$ 231,092	$ 983,830	$ 717,486

Total revenues include net product revenues attributed to geographic regions based on the ship-to location and license and collaboration services revenues attributed to geographic regions based on the location of our collaboration partners' headquarters.

Net product revenues and license revenues are recorded in accordance with ASC Topic 606, *Revenue from Contracts with Customers* (Topic 606). License revenues include the recognition of the portion of milestone payments allocated to the transfer of intellectual property licenses for which it had become probable in the current period that the milestone would be achieved and a significant reversal of revenues would not occur, as well as royalty revenues and our share of profits under our collaboration agreement with Genentech. Collaboration services revenues were recorded in accordance with ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606* and by analogy to Topic 606. Collaboration services revenues include the recognition of deferred revenues for the portion of upfront and milestone payments allocated to our research and development services performance obligations, development cost reimbursements earned under our collaboration agreements, product supply revenues, net of product supply costs, and the royalties we paid on sales of products containing cabozantinib by our collaboration partners. We received notification that, effective January 1, 2021, Royalty Pharma plc (Royalty Pharma) acquired from GlaxoSmithKline (GSK) all rights, title and interest in royalties on net product sales containing cabozantinib for non-U.S. markets for the full term of the royalty and for the U.S. market through September 2026, after which time U.S. royalties will revert back to GSK.

Net product revenues by product were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
CABOMETYX	$ 259,791	$ 159,555	$ 759,000	$ 522,381
COMETRIQ	3,326	9,032	15,577	18,816
Net product revenues	$ 263,117	$ 168,587	$ 774,577	$ 541,197

Product Sales Discounts and Allowances

The activities and ending reserve balances for each significant category of discounts and allowances, which constitute variable consideration, were as follows (in thousands):

	Chargebacks, Discounts for Prompt Payment and Other	Other Customer Credits/Fees and Co-pay Assistance	Rebates	Total
Balance at December 31, 2020	$ 9,853	$ 3,279	$ 17,404	$ 30,536
Provision related to sales made in:				
Current period	178,083	22,945	74,851	275,879
Prior periods	(22)	(225)	1,662	1,415
Payments and customer credits issued	(171,416)	(18,789)	(70,007)	(260,212)
Balance at September 30, 2021	$ 16,498	$ 7,210	$ 23,910	$ 47,618

The allowance for chargebacks, discounts for prompt payment and other are recorded as a reduction of trade receivables, net and the remaining reserves are recorded as rebates and fees due to customers in the accompanying Condensed Consolidated Balance Sheets.

Contract Assets and Liabilities

We receive payments from our collaboration partners based on billing schedules established in each contract. Amounts are recorded as accounts receivable when our right to consideration is unconditional. We may also recognize revenue in advance of the contractual billing schedule and such amounts are recorded as a contract asset when recognized. We may be required to defer recognition of revenue for upfront and milestone payments until we perform our obligations under these arrangements, and such amounts are recorded as deferred revenue upon receipt or when due. For those contracts that have multiple performance obligations, contract assets and liabilities are reported on a net basis at the contract level. Contract assets were zero as of September 30, 2021 and December 31, 2020. Contract liabilities as of September 30, 2021 are primarily related to deferred revenues from Takeda Pharmaceutical Company Limited (Takeda).

Contract liabilities were as follows (in thousands):

	September 30, 2021	December 31, 2020
Contract liabilities:		
Current portion [1]	$ 7,535	$ 1,790
Long-term portion [1]	9,444	3,755
Total contract liabilities	$ 16,979	$ 5,545

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(1) Presented in Other current liabilities and Long-term portion of deferred revenues, respectively, in the accompanying Condensed Consolidated Balance Sheets.

We recognized $6.8 million in revenues in each of the nine months ended September 30, 2021 and 2020, that were included in the beginning deferred revenues balance for those periods.

During the three and nine months ended September 30, 2021, we recognized $48.4 million and $116.2 million, respectively, in revenues for performance obligations satisfied in previous periods, as compared to $33.1 million and $115.3 million for the corresponding periods in 2020. Such revenues were primarily related to royalty payments allocated to the license performance obligations for our collaborations with Ipsen Pharma SAS (Ipsen), Takeda, Daiichi Sankyo and Genentech.

As of September 30, 2021, $86.5 million of the combined transaction prices for our Ipsen and Takeda collaborations were allocated to performance obligations that had not yet been satisfied. See “Note 3. Collaboration Agreements— Cabozantinib Collaborations - Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations” to our Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2020 for information about the expected timing to satisfy these performance obligations.

NOTE 3. COLLABORATION AGREEMENTS, IN-LICENSING ARRANGEMENTS AND BUSINESS DEVELOPMENT ACTIVITIES

We have established multiple collaborations with leading pharmaceutical companies for the commercialization and further development of our cabozantinib franchise. Additionally, we have entered into several research collaboration and in-licensing arrangements to further enhance our early-stage pipeline and expand our ability to discover, develop and commercialize novel therapies with the goal of providing new treatment options for cancer patients and their physicians. Historically, we also entered into other collaborations with leading pharmaceutical companies pursuant to which we out-licensed other compounds and programs in our portfolio.

See “Note 3. Collaboration Agreements” to our Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, or as further described below, for additional information on each of our collaboration agreements and in-licensing arrangements.

Cabozantinib Collaborations

Ipsen Collaboration

In February 2016, we entered into a collaboration agreement with Ipsen for the commercialization and further development of cabozantinib. Under the terms of the collaboration agreement, as amended, Ipsen received exclusive commercialization rights for current and potential future cabozantinib indications outside of the U.S. and Japan. We have also agreed to collaborate with Ipsen on the development of cabozantinib for current and potential future indications. The parties’ efforts are governed through a joint steering committee and appropriate subcommittees established to guide and oversee the collaboration’s operation and strategic direction; provided, however, that we retain final decision-making authority with respect to cabozantinib’s ongoing development.

During the second quarter of 2021, Ipsen opted into and is now co-funding the development costs for COSMIC-311, our phase 3 pivotal trial evaluating cabozantinib versus placebo in patients with RAI-refractory DTC who have progressed after up to two VEGF receptor-targeted therapies. Under the terms of the collaboration agreement, Ipsen is now obligated to reimburse us for their share of COSMIC-311 global development costs, as well as an additional payment calculated as a percentage of such costs, triggered by the timing of the exercise of its option. We determined that the decision to opt in and co-fund the development costs for COSMIC-311 represented a contract modification for additional distinct services at their standalone selling price and therefore was treated as a separate contract under Topic 606.

Accordingly, collaboration services revenues for the nine months ended September 30, 2021, includes a cumulative catch up for Ipsen's share of global development costs incurred since the beginning of the study and through the end of the period.

Revenues under the collaboration agreement with Ipsen were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
License revenues	$ 25,139	$ 19,910	$ 81,246	$ 71,456
Collaboration services revenues	12,956	16,096	81,576	46,503
Total	$ 38,095	$ 36,006	$ 162,822	$ 117,959

Milestone revenues for the nine months ended September 30, 2021 included $11.9 million recognized in connection with a $12.5 million regulatory milestone we determined was probable of achievement in the second quarter of 2021. The milestone was achieved in the third quarter of 2021 upon submission of a variation application to the European Medicines Agency for CABOMETYX as a treatment for patients with previously treated RAI-refractory DTC.

As of September 30, 2021, $44.8 million of the transaction price was allocated to our research and development services performance obligations that has not yet been satisfied.

Takeda Collaboration

In January 2017, we entered into a collaboration and license agreement with Takeda for the commercialization and further development of cabozantinib. Pursuant to this collaboration and license agreement, as amended, Takeda has exclusive commercialization rights for current and potential future cabozantinib indications in Japan, and the parties have agreed to collaborate on the clinical development of cabozantinib in Japan. The operation and strategic direction of the parties' collaboration is governed through a joint executive committee and appropriate subcommittees.

Revenues under the collaboration agreement with Takeda were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
License revenues	$ 20,078	$ 9,780	$ 23,476	$ 32,726
Collaboration services revenues	2,656	13,204	10,815	16,468
Total	$ 22,734	$ 22,984	$ 34,291	$ 49,194

Milestone revenues for the three and nine months ended September 30, 2021 included $18.8 million recognized in connection with a $20.0 million milestone we achieved upon Takeda's first commercial sale in Japan of CABOMETYX in combination with OPDIVO for the treatment of patients with unresectable, advanced or metastatic RCC.

As of September 30, 2021, $41.7 million of the transaction price was allocated to our research and development services performance obligations that has not yet been satisfied.

GSK and Royalty Pharma

In October 2002, we established a product development and commercialization collaboration agreement with GSK, that required us to pay a 3% royalty to GSK on the worldwide net sales of any product incorporating cabozantinib by us and our collaboration partners. As disclosed in Note 2, we received notification that, effective January 1, 2021, Royalty Pharma acquired from GSK all rights, title and interest in royalties on net product sales containing cabozantinib for non-U.S. markets for the full term of the royalty and for U.S. market through September 2026, after which time U.S. royalties will revert back to GSK. Royalties earned by GSK and Royalty Pharma in connection with our sales of cabozantinib are included in cost of goods sold and as a reduction of collaboration services revenues for sales by our collaboration partners. Such royalties were $11.5 million and $33.7 million during the three and nine months ended September 30, 2021, respectively, as compared to $7.9 million and $23.7 million in the corresponding periods in 2020.

Genentech Collaboration

In December 2006, we out-licensed the development and commercialization of cobimetinib to Genentech under a worldwide collaboration agreement. In November 2015, the FDA approved cobimetinib, under the brand name COTELLIC, in combination with Genentech's ZELBORAF® (vemurafenib) for the treatment of patients with BRAF V600E or V600K mutation-positive advanced melanoma. COTELLIC in combination with ZELBORAF has also been approved in the European Union and multiple additional countries for use in the same indication. In July 2020, the FDA also approved COTELLIC for use in combination with ZELBORAF and TECENTRIQ® (atezolizumab) for the treatment of patients with BRAF V600 mutation-positive advanced melanoma in previously untreated patients. License revenues under the collaboration agreement with Genentech were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Profits on U.S. commercialization	$ 1,743	$ 1,595	$ 5,697	$ 4,378
Royalty revenues on ex-U.S. sales	$ 1,576	$ 1,370	$ 3,309	$ 3,804

Research Collaborations, In-Licensing Arrangements and Other Business Development Activities

During the nine months ended September 30, 2021, in support of our development pipeline, we entered into collaboration and in-licensing arrangements with Adagene Inc. (Adagene), WuXi Biologics Ireland Limited (WuXi Bio), expanded our collaboration with Invenra, Inc. (Invenra), and amended our existing collaboration agreement with StemSynergy Therapeutics, Inc. (StemSynergy). In conjunction with each of these arrangements we have made aggregate upfront payments totaling $28.0 million and will make payments for potential future development milestones of up to $98.0 million, regulatory milestones of up to $229.0 million and commercial milestones of up to $802.5 million, each in the aggregate per product or target, as well as royalties on future net product sales. In addition to the upfront and future milestone payments, we will also pay Invenra, in three equal annual installments, an exclusivity payment of up to $15.0 million to nominate up to 20 additional oncology targets and up to $30.0 million in research program funding in equal quarterly payments over a three-year period, as well as additional fees. As of September 30, 2021, we have paid the first exclusivity installment of $5.0 million and $2.5 million for the first quarterly research and development funding installment. We have the ability to opt in to certain of Invenra's other internal research programs in exchange for an option exercise payment of $3.0 million per program.

Additionally, in May 2021, we entered into an asset purchase agreement with GamaMabs Pharma SA (GamaMabs), pursuant to which we made an upfront payment of $5.0 million for the initial technology transfer, and subject to certain conditions, will make a $9.0 million payment upon the completion of an initial technology transfer of certain materials and documents specified in the asset purchase agreement. We will also make payments for potential future development milestones of up to $42.0 million and regulatory milestones of up to $22.5 million, per product.

NOTE 4. CASH AND INVESTMENTS

Cash, Cash Equivalents and Restricted Cash Equivalents

A reconciliation of cash, cash equivalents, and restricted cash equivalents reported in the accompanying Condensed Consolidated Balance Sheets to the amount reported within the accompanying Condensed Consolidated Statements of Cash Flows was as follows (in thousands):

	September 30, 2021	December 31, 2020
Cash and cash equivalents	$ 567,325	$ 319,217
Restricted cash equivalents included in other long-term assets	31,163	1,555
Cash, cash equivalents, and restricted cash equivalents as reported in the accompanying Condensed Consolidated Statements of Cash Flows	$ 598,488	$ 320,772

Restricted cash equivalents are used to collateralize letters of credit and consist of money-market funds and certificates of deposit with original maturities of 90 days or less. The restricted cash equivalents are classified as other long-term assets based upon the remaining term of the underlying restriction. As of September 30, 2021, restricted cash equivalents included $29.6 million of short-term investments, which is collateral under our January 2021 standby letter of credit to guarantee our obligation to fund a portion of the total tenant improvements related to our build-to-suit lease at our corporate campus. As we fund these tenant improvements, our restricted cash becomes available for operations.

Cash, Cash Equivalents, Restricted Cash Equivalents and Investments

Cash, cash equivalents, restricted cash equivalents and investments consisted of the following (in thousands):

	September 30, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Debt securities available-for-sale:				
Commercial paper	$ 886,323	$ 73	$ —	$ 886,396
Corporate bonds	503,707	1,967	(126)	505,548
U.S. Treasury and government-sponsored enterprises	58,965	21	(1)	58,985
Municipal bonds	10,670	41	—	10,711
Total debt securities available-for-sale	1,459,665	2,102	(127)	1,461,640
Cash	80,828	—	—	80,828
Money market funds	119,538	—	—	119,538
Certificates of deposit	134,106	—	—	134,106
Total cash, cash equivalents, restricted cash equivalents and investments	$ 1,794,137	$ 2,102	$ (127)	$ 1,796,112

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Debt securities available-for-sale:				
Commercial paper	$ 569,456	$ 372	$ —	$ 569,828
Corporate bonds	543,520	5,244	(7)	548,757
U.S. Treasury and government-sponsored enterprises	208,326	232	(4)	208,554
Municipal bonds	28,680	83	(1)	28,762
Total debt securities available-for-sale	1,349,982	5,931	(12)	1,355,901
Cash	82,176	—	—	82,176
Money market funds	40,761	—	—	40,761
Certificates of deposit	60,004	—	—	60,004
Total cash, cash equivalents, restricted cash equivalents and investments	$ 1,532,923	$ 5,931	$ (12)	$ 1,538,842

Interest receivable was $2.6 million and $4.5 million as of September 30, 2021 and December 31, 2020, respectively, and is included in prepaid expenses and other current assets in the accompanying Condensed Consolidated Balance Sheets.

Realized gains and losses on the sales of investments were insignificant during the three and nine months ended September 30, 2021 and 2020.

We manage credit risk associated with our investment portfolio through our investment policy, which limits purchases to high-quality issuers and limits the amount of our portfolio that can be invested in a single issuer. The fair value and gross unrealized losses on debt securities available-for-sale in an unrealized loss position were as follows (in thousands):

	September 30, 2021	
	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 136,319	$ (126)
U.S. Treasury and government-sponsored enterprises	10,007	(1)
Total	$ 146,326	$ (127)

	December 31, 2020	
	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 28,445	$ (7)
U.S. Treasury and government-sponsored enterprises	21,989	(4)
Municipal bonds	5,865	(1)
Total	$ 56,299	$ (12)

All securities presented have been in an unrealized loss position for less than 12 months. There were 41 and 14 investments in an unrealized loss position as of September 30, 2021 and December 31, 2020, respectively. During the nine months ended September 30, 2021 and 2020, we did not record an allowance for credit losses or other impairment charges on our investment securities. Based upon our quarterly impairment review, we determined that the unrealized losses were not attributed to credit risk but were primarily associated with changes in interest rates and market liquidity. Based on the scheduled maturities of our investments, we determined that it was more likely than not that we will hold these investments for a period of time sufficient for a recovery of our cost basis.

The fair value of debt securities available-for-sale by contractual maturity was as follows (in thousands):

	September 30, 2021	December 31, 2020
Maturing in one year or less	$ 1,103,122	$ 1,034,150
Maturing after one year through five years	358,518	321,751
Total debt securities available-for-sale	$ 1,461,640	$ 1,355,901

NOTE 5. FAIR VALUE MEASUREMENTS

Fair value reflects the amounts that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value hierarchy has the following three levels:

- Level 1 - quoted prices (unadjusted) in active markets for identical assets and liabilities;
- Level 2 - inputs other than level 1 that are observable either directly or indirectly, such as quoted prices in active markets for similar instruments or on industry models using data inputs, such as interest rates and prices that can be directly observed or corroborated in active markets; and
- Level 3 - unobservable inputs that are supported by little or no market activity that are significant to the fair value measurement.

The classifications within the fair value hierarchy of our financial assets that were measured and recorded at fair value on a recurring basis were as follows (in thousands):

	September 30, 2021		
	Level 1	Level 2	Total
Commercial paper	$ —	$ 886,396	$ 886,396
Corporate bonds	—	505,548	505,548
U.S. Treasury and government-sponsored enterprises	—	58,985	58,985
Municipal bonds	—	10,711	10,711
Total debt securities available-for-sale	—	1,461,640	1,461,640
Money market funds	119,538	—	119,538
Certificates of deposit	—	134,106	134,106
Total financial assets carried at fair value	$ 119,538	$ 1,595,746	$ 1,715,284

	December 31, 2020		
	Level 1	Level 2	Total
Commercial paper	$ —	$ 569,828	$ 569,828
Corporate bonds	—	548,757	548,757
U.S. Treasury and government-sponsored enterprises	—	208,554	208,554
Municipal bonds	—	28,762	28,762
Total debt securities available-for-sale	—	1,355,901	1,355,901
Money market funds	40,761	—	40,761
Certificates of deposit	—	60,004	60,004
Total financial assets carried at fair value	$ 40,761	$ 1,415,905	$ 1,456,666

When available, we value investments based on quoted prices for those financial instruments, which is a Level 1 input. Our remaining investments are valued using third-party pricing sources, which use observable market prices, interest rates and yield curves observable at commonly quoted intervals for similar assets as observable inputs for pricing, which is a Level 2 input.

The carrying amount of our remaining financial assets and liabilities, which include cash, receivables and payables, approximate their fair values due to their short-term nature.

Forward Foreign Currency Contracts

In January 2021, we initiated an operational hedging program and entered into forward contracts to hedge certain operational exposures for the changes in foreign currency exchanges rates associated with assets or liabilities denominated in foreign currencies, primarily the Euro.

As of September 30, 2021, we had one forward contract outstanding to sell €9.8 million. The forward contract with a maturity of three months is recorded at fair value and is included in prepaid expenses and other current assets in the Condensed Consolidated Balance Sheets. The unrealized gain/loss on the settlement of the forward contract is not material as of September 30, 2021. The forward contract is considered a Level 2 in the fair value hierarchy of our fair value measurements. For the nine months ended September 30, 2021, we recognized $0.5 million of net gains on the maturity of our forward contracts, which is included in other income (expense), net on our Condensed Consolidated Statements of Income (Loss).

NOTE 6. INVENTORY

Inventory consisted of the following (in thousands):

	September 30, 2021	December 31, 2020
Raw materials	$ 10,317	$ 7,773
Work in process	28,016	20,610
Finished goods	11,707	7,291
Total	$ 50,040	$ 35,674
Balance Sheet classification:		
Current portion included in inventory	$ 28,240	$ 20,973
Long-term portion included in other long-term assets	21,800	14,701
Total	$ 50,040	$ 35,674

NOTE 7. STOCK-BASED COMPENSATION

We allocated the stock-based compensation expense for our equity incentive plans and our Employee Stock Purchase Plan (ESPP) as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Research and development	$ 11,487	$ 18,936	$ 37,550	$ 30,134
Selling, general and administrative	22,479	36,719	59,104	55,657
Total stock-based compensation expense	$ 33,966	$ 55,655	$ 96,654	$ 85,791

Stock-based compensation for each type of award under our equity incentive plans and ESPP were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Stock options	$ 4,607	$ 5,021	$ 15,203	$ 15,316
Restricted stock units	13,721	8,816	40,802	25,212
Performance stock units	14,971	41,226	37,616	43,151
ESPP	667	592	3,033	2,112
Total stock-based compensation expense	$ 33,966	$ 55,655	$ 96,654	$ 85,791

As of September 30, 2021, 9,248,609 shares were available for grant under the Exelixis, Inc. 2017 Equity Incentive Plan (as amended and restated, the 2017 Plan). The share reserve is reduced by 1 share for each share issued pursuant to a stock option and 1.5 shares for full value awards granted in the form of restricted stock units (RSUs).

During the nine months ended September 30, 2021, we granted 2,032,884 stock options with a weighted average exercise price of $21.81 per share and a weighted average grant date fair value of $9.30 per share. As of September 30, 2021, there were 14,357,896 stock options outstanding and $28.6 million of related unrecognized compensation expense.

During the nine months ended September 30, 2021, we granted 3,947,355 service-based RSUs with a weighted average grant date fair value of $21.50 per share. As of September 30, 2021, there were 8,218,085 RSUs outstanding and $136.3 million of related unrecognized compensation expense.

Stock options and RSUs granted to employees during the nine months ended September 30, 2021 have vesting conditions and contractual lives of a similar nature to those described in “Note 8. Employee Benefit Plans” of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

In March 2021, we awarded 1,027,650 (the target amount) performance-based (PSUs), subject to a performance and a market condition (the 2021 PSUs). Pursuant to the terms of 2021 PSUs, the holders of the awards may earn up to 200% of the target amount of shares, depending on the level of achievement of the performance condition related to certain net product revenues and a total shareholder return (TSR) market condition. The TSR market condition is based on our relative TSR percentile rank compared to companies in the NASDAQ Biotechnology Index during the performance period, which is January 2, 2021 through December 29, 2023. Fifty percent of the shares earned subject to the performance and market conditions will vest at the end of the performance period and the remainder will vest approximately one year later subject to an employee's continuous service. The 2021 PSUs will be forfeited if the performance condition at or above a threshold level is not achieved by December 29, 2023.

A Monte Carlo simulation model was used to determine the grant date fair value of $24.54 for the 2021 PSUs based on the following assumptions:

Fair value of the Company's common stock on grant date	$ 21.31
Expected volatility	49 %
Risk-free interest rate	0.29 %
Dividend yield	— %

The Monte Carlo simulation model also assumed correlations of returns of the stock prices of the Company's common stock and the common stock of a peer group of companies and historical stock price volatility of the peer group of companies. The valuation model also used terms based on the length of the performance period and compound annual growth rate goals for total stockholder return based on the provisions of the award.

As of September 30, 2021, there were 7,768,188 PSUs outstanding and $128.6 million of related unrecognized stock-based compensation expense. Expense recognition for PSUs commences when it is determined that achievement of the performance target is probable. During the three months ended September 30, 2021, we achieved an additional performance target for 524,307 PSUs granted during 2020 (the 2020 PSUs) and determined that it had become probable that we would achieve an additional performance target for 167,726 PSUs granted during 2018 (the 2018 PSUs) and have recognized $11.4 million of stock-based compensation expense related to the 2020 PSUs and 2018 PSUs during the three months ended September 30, 2021. For more information about our PSUs, see "Note 8. Employee Benefit Plans" of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

NOTE 8. PROVISION FOR (BENEFIT FROM) INCOME TAXES

The effective tax rate for the three and nine months ended September 30, 2021 was 28.3% and 22.8%, respectively, as compared to 15.7% and 18.8% for the corresponding periods in 2020. The effective tax rate for the three and nine months ended September 30, 2021 differed from the U.S. federal statutory tax rate of 21% primarily due to non-deductible executive compensation, partially offset by excess tax benefits related to the exercise of certain stock options during the periods and the generation of federal tax credits. The effective tax rate for the three and nine months ended September 30, 2020 differed from the U.S. federal statutory tax rate of 21% primarily due to excess tax benefits related to the exercise of certain stock options, the generation of federal tax credits, partially offset by non-deductible executive compensation during the periods.

NOTE 9. NET INCOME (LOSS) PER SHARE

Net income (loss) per share - basic and diluted, were computed as follows (in thousands, except per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Numerator:				
Net income (loss)	$ 38,204	$ (32,040)	$ 135,897	$ 83,393
Denominator:				
Weighted-average common shares outstanding — basic	315,380	309,116	313,990	307,437
Dilutive securities	6,642	—	8,094	10,058
Weighted-average common shares outstanding — diluted	322,022	309,116	322,084	317,495
Net income (loss) per share — basic	$ 0.12	$ (0.10)	$ 0.43	$ 0.27
Net income (loss) per share — diluted	$ 0.12	$ (0.10)	$ 0.42	$ 0.26

Dilutive securities included outstanding stock options, Performance Stock Options, unvested RSUs, PSUs and ESPP contributions.

Certain potential common shares were excluded from our calculation of weighted-average common shares outstanding - diluted because either they would have had an anti-dilutive effect on net income per share or they were related to shares from PSUs that were contingently issuable and the contingency had not been satisfied at the end of the reporting period. The weighted-average potential common shares excluded from our calculation were as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Anti-dilutive securities and contingently issuable shares excluded	20,346	27,033	14,213	10,224

NOTE 10. COMMITMENTS AND CONTINGENCIES

In September 2019, we received a notice letter regarding an Abbreviated New Drug Application (ANDA) submitted to the FDA by MSN Pharmaceuticals, Inc. (MSN), requesting approval to market a generic version of CABOMETYX tablets. MSN's initial notice letter included a Paragraph IV certification with respect to our U.S. Patent Nos. 8,877,776, 9,724,342, 10,034,873 and 10,039,757, which are listed in the Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book, for CABOMETYX. MSN's initial notice letter did not provide a Paragraph IV certification against U.S. Patent No. 7,579,473, the composition of matter patent, or U.S. Patent No. 8,497,284, a method of use patent, each of which is listed in the Orange Book. On October 29, 2019, we filed a complaint in the United States District Court for the District of Delaware (the Delaware District Court) for patent infringement against MSN asserting U.S. Patent No. 8,877,776 arising from MSN's ANDA filing with the FDA. On November 20, 2019, MSN filed its response to the complaint, alleging that U.S. Patent No. 8,877,776 is invalid and not infringed. On May 5, 2020, we received notice from MSN that it had amended its ANDA to assert additional Paragraph IV certifications. The ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of the two previously unasserted CABOMETYX patents: U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284. On May 11, 2020, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284 arising from MSN's amended ANDA filing with the FDA. Neither of our complaints alleges infringement of U.S. Patent Nos. 9,724,342, 10,034,873 and 10,039,757. On May 22, 2020, MSN filed its response to the complaint, alleging that each of U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284 is invalid and not infringed. On March 23, 2021, MSN filed its First Amended Answer and Counterclaims (amending its prior filing from May 22, 2020), seeking, among other things, a declaratory judgment that U.S. Patent No. 9,809,549 is invalid and would not be infringed by MSN if its generic version of CABOMETYX tablets were approved by the FDA. U.S. Patent No. 9,809,549 is not listed in the Orange Book. On April 7, 2021, we filed our response to MSN's First Amended Answer and Counterclaims, denying, among other things, that U.S. Patent No. 9,809,549 is invalid or would not be infringed.

On October 1, 2021, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patent Nos. 7,579,473 and 8,497,284, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patent Nos. 7,579,473 and 8,497,284 would also infringe certain claims of each patent, if those claims are not found to be invalid. Then, on October 12, 2021, pursuant to a separate stipulation between us and MSN, the Delaware District Court entered an order dismissing MSN's counterclaims with respect to U.S. Patent No. 9,809,549. In our complaints, we are seeking, among other relief, an order that the effective date of any FDA approval of MSN's ANDA be a date no earlier than the expiration of all of U.S. Patent No. 7,579,473, U.S. Patent No. 8,497,284 and U.S. Patent No. 8,877,776, the latest of which expires on October 8, 2030, and equitable relief enjoining MSN from infringing these patents. These lawsuits against MSN have been consolidated, and a bench trial has been scheduled for May 2022.

In May 2021, we received notice letters from Teva Pharmaceuticals Development, Inc. and Teva Pharmaceuticals USA, Inc. (individually and collectively referred to as Teva) regarding an ANDA Teva submitted to the FDA, requesting approval to market a generic version of CABOMETYX tablets. Teva's notice letters included a Paragraph IV certification with respect to our U.S. Patent Nos. 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Orange Book and expire in 2033, 2031 and 2031, respectively. Teva's notice letters did not provide a Paragraph IV certification against any additional CABOMETYX patents. On June 17, 2021, we filed a complaint in the Delaware District Court for patent infringement against Teva, along with Teva Pharmaceutical Industries Limited (Teva Parent), asserting U.S. Patent Nos. 9,724,324 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment) arising from Teva's ANDA filing with the FDA. On August 27, 2021, Teva filed its answer and counterclaims to the complaint, alleging that all of U.S. Patent Nos. 9,724,324, 10,034,873 and 10,039,757 are invalid and not infringed, and on August 23, 2021, we and Teva entered into a stipulation wherein Teva Parent was dismissed without prejudice from this lawsuit and agreed to be bound by any stipulation, judgment, order or decision rendered as to Teva, including any appeals and any order granting preliminary or permanent injunctive relief against Teva. On September 17, 2021, we filed an answer to Teva's counterclaims. We are seeking, among other relief, an order that the effective date of any FDA approval of Teva's ANDA be a date no earlier than the expiration of all of U.S. Patent Nos. 9,724,342, 10,034,873 and 10,039,757, the latest of which expires on July 9, 2033, and equitable relief enjoining Teva from infringing these patents. A bench trial has been scheduled for June 2023.

The sale of any generic version of CABOMETYX earlier than its patent expiration could significantly decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations. It is not possible at this time to determine the likelihood of an unfavorable outcome or estimate of the amount or range of any potential loss.

We may also from time to time become a party or subject to various other legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. Some of these proceedings have involved, and may involve in the future, claims that are subject to substantial uncertainties and unascertainable damages.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

This Quarterly Report on Form 10-Q contains forward-looking statements. These statements are based on Exelixis, Inc.'s (Exelixis, we, our or us) current expectations, assumptions, estimates and projections about our business and our industry and involve known and unknown risks, uncertainties and other factors that may cause our company's or our industry's results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied in, or contemplated by, the forward-looking statements. Our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include those discussed in "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q, as well as those discussed elsewhere in this report. These and many other factors could affect our future financial and operating results. We undertake no obligation to update any forward-looking statement to reflect events after the date of this report.

This discussion and analysis should be read in conjunction with our condensed consolidated financial statements and accompanying notes included in this report and the consolidated financial statements and accompanying notes thereto *included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 submitted to the Securities and Exchange Commission (SEC) on February 10, 2021.*

Overview

We are an oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. We have invented and brought to market novel, effective and tolerable therapies using our drug discovery and development resources and capabilities and commercialization platform; we will continue to build on this foundation, working toward providing cancer patients with additional treatment options.

Since our founding in 1994, four products resulting from our discovery efforts have progressed through clinical development, received regulatory approval and established a commercial presence in various geographies around the world. Our flagship molecule, cabozantinib, is an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET and has been approved by the U.S. Food and Drug Administration (FDA) and foreign regulatory authorities as two products: CABOMETYX® (cabozantinib) tablets approved for advanced renal cell carcinoma (RCC), both alone and in combination with Bristol-Myers Squibb Company's (BMS) OPDIVO® (nivolumab), for previously treated hepatocellular carcinoma (HCC) and, in the U.S. only, for previously treated, radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC); and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer (MTC). For these types of cancer, cabozantinib has become or is becoming a standard of care.

The other two products resulting from our discovery efforts are: COTELLIC® (cobimetinib), an inhibitor of MEK, approved as part of multiple combination regimens to treat specific forms of advanced melanoma and marketed under a collaboration with Genentech, Inc. (a member of the Roche Group) (Genentech); and MINNEBRO® (esaxerenone), an oral, non-steroidal, selective blocker of the mineralocorticoid receptor, approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo Company, Limited (Daiichi Sankyo).

Leveraging the revenue stream derived from our cabozantinib franchise and other marketed products, we are expanding our oncology product pipeline through drug discovery efforts, which encompass both small molecule and biologics programs with multiple modalities and mechanisms of action.

Cabozantinib Franchise

On January 22, 2021, the FDA approved CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC. This regulatory milestone expands upon the FDA's prior approvals of CABOMETYX as a monotherapy for previously treated patients with advanced RCC in April 2016 and for previously untreated patients with advanced RCC in December 2017. Additionally, in January 2019, the FDA approved CABOMETYX for the treatment of patients with HCC who have been previously treated with sorafenib, and most recently, on September 17, 2021, the FDA approved CABOMETYX for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic DTC that has progressed following prior VEGF receptor-targeted therapy and who are RAI-refractory or ineligible.

To develop and commercialize CABOMETYX and COMETRIQ outside the U.S., we have entered into license agreements with Ipsen Pharma SAS (Ipsen) and Takeda Pharmaceutical Company Limited (Takeda). We granted to Ipsen the rights to develop and commercialize cabozantinib outside of the U.S. and Japan, and to Takeda the rights to develop and commercialize cabozantinib in Japan. Both Ipsen and Takeda also contribute financially and operationally to the further global development and commercialization of the cabozantinib franchise in other potential indications, and we continue to work closely with them on these activities. Utilizing its regulatory expertise and established international oncology marketing network, Ipsen has continued to execute on its commercialization plans for CABOMETYX, having received regulatory approvals and launched in multiple territories outside of the U.S., including in the European Union (EU) and Canada, as a treatment for advanced RCC and for HCC in adults who have previously been treated with sorafenib. In addition, in March 2021, Ipsen and BMS received regulatory approval from the European Commission (EC) for CABOMETYX in combination with OPDIVO as a first-line treatment for patients with advanced RCC, and both Ipsen and BMS plan to submit applications to approve the combination in other territories beyond the EU. Ipsen also submitted a variation application to the European Medicines Agency (EMA) to approve CABOMETYX as a treatment for patients with previously treated, RAI-refractory DTC, with the EMA validating the variation and beginning its centralized review process in August 2021. With respect to the Japanese market, Takeda received Manufacturing and Marketing Approvals in 2020 from the Japanese Ministry of Health, Labour and Welfare (MHLW) of CABOMETYX as a treatment of patients with curatively unresectable or metastatic RCC and as a treatment of patients with unresectable HCC who progressed after cancer chemotherapy. Most recently, in August 2021, Takeda and Ono Pharmaceutical Co., Ltd. (Ono), BMS' development and commercialization partner in Japan, received Manufacturing and Marketing Approval from the Japanese MHLW of CABOMETYX in combination with OPDIVO as a treatment for unresectable or metastatic RCC.

In addition to our regulatory and commercialization efforts in the U.S. and the support provided to our collaboration partners for rest-of-world regulatory and commercialization activities, we are also pursuing other indications for cabozantinib that have the potential to increase the number of cancer patients who could benefit from this medicine. We are evaluating cabozantinib, both as a single agent and in combination with other therapies, in a broad development program comprising over 100 ongoing or planned clinical trials across multiple indications. We, along with our collaboration partners, sponsor some of the trials, and independent investigators conduct the remaining trials through our Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute's Cancer Therapy Evaluation Program (NCI-CTEP) or our investigator-sponsored trial (IST) program. Informed by the available data from these clinical trials, we advanced the development program for the cabozantinib franchise with potentially label-enabling trials.

One pivotal trial that has resulted from this effort is COSMIC-311, our phase 3 pivotal trial evaluating cabozantinib versus placebo in patients with RAI-refractory DTC who have progressed after up to two VEGF receptor-targeted therapies. In December 2020, we announced that COSMIC-311 had met the primary endpoint of demonstrating significant improvement in progression-free survival (PFS), which served as the basis for the FDA's September 2021 DTC approval for CABOMETYX. Study results from COSMIC-311 were presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting and at the European Society of Medical Oncology (ESMO) 2021 Congress, as well as published in *The Lancet Oncology*.

Building on preclinical and clinical observations that cabozantinib in combination with immune checkpoint inhibitors (ICIs) may promote a more immune-permissive tumor environment, we initiated numerous pivotal studies to further explore these combination regimens. The first of these studies to deliver results was CheckMate -9ER, a phase 3 pivotal trial evaluating the combination of cabozantinib and nivolumab compared to sunitinib in previously untreated advanced or metastatic RCC. We, along with our collaboration partner, BMS, announced in April 2020 that the trial met its primary endpoint of PFS at final analysis, as well as the secondary endpoints of overall survival (OS) at a pre-specified interim analysis and objective response rate (ORR), and showed that the combination of cabozantinib with nivolumab significantly improved the three key efficacy outcomes as compared with sunitinib, doubling PFS and ORR and reducing the risk of disease progression or death by 40% compared with sunitinib. Data from CheckMate -9ER served as the basis for the FDA's and EC's approval of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC in January 2021 and March 2021, respectively. We are also collaborating with BMS on COSMIC-313, a phase 3 pivotal trial evaluating the triplet combination of cabozantinib, nivolumab and ipilimumab versus the combination of nivolumab and ipilimumab in patients with previously untreated advanced intermediate- or poor-risk RCC. Enrollment for COSMIC-313 was completed in March 2021, and we expect to report top-line results of the event-driven analyses from the trial in the late 2021 or early 2022 timeframe.

To expand our exploration of combinations with ICIs, we also initiated multiple trials evaluating cabozantinib in combination with F. Hoffmann-La Roche Ltd.'s (Roche) ICI, atezolizumab. COSMIC-021 is a broad phase 1b study evaluating the safety and tolerability of cabozantinib in combination with atezolizumab in patients with a wide variety of locally advanced or metastatic solid tumors. Based on encouraging efficacy and safety data that has emerged from the trial, certain cohorts have been or may be further expanded, including the cohorts of patients with non-small cell lung cancer (NSCLC) who have been previously treated with an ICI and metastatic castration-resistant prostate cancer (mCRPC) who have been previously treated with enzalutamide and/or abiraterone acetate and experienced radiographic disease progression in soft tissue (Cohort 6). Data from Cohort 6, announced in May 2021, resulted in an investigator assessed ORR of 27% and a blinded independent radiology committee (BIRC) assessed ORR of 18%. Detailed results from Cohort 6, including PFS data in the high-risk patient population, were presented at the ESMO 2021 Congress.

Although, following our discussions with the FDA, we will not pursue a regulatory submission for the combination regimen based on Cohort 6, data from COSMIC-021 have been instrumental in guiding our clinical development strategy for cabozantinib in combination with ICIs, including supporting the initiation of COSMIC-312, a phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus sorafenib in previously untreated advanced HCC, and three phase 3 pivotal trials in collaboration with Roche, CONTACT-01, CONTACT-02 and CONTACT-03, evaluating the combination of cabozantinib with atezolizumab in patients with metastatic NSCLC, mCRPC and advanced RCC, respectively. CONTACT-01 and CONTACT-03 are sponsored by Roche and co-funded by us; CONTACT-02 is sponsored by us and co-funded by Roche. In June 2021, we announced results from COSMIC-312. The trial met one of the primary endpoints, demonstrating significant improvement in PFS at the planned primary analysis, reducing the risk of disease progression or death by 37% compared with sorafenib (hazard ratio: 0.63; 99% confidence internal: 0.44-0.91; P=0.0012). A prespecified interim analysis for the second primary endpoint of OS, conducted at the same time as the primary analysis for PFS, showed a trend favoring the combination of cabozantinib and atezolizumab but did not reach statistical significance. Safety for the combination appeared to be consistent with the known safety profiles of the individual medicines, and no new safety signals were identified. Based on the preliminary OS data, we anticipate that the probability of reaching statistical significance at the time of the final analysis is low, but the trial will continue as planned to the final analysis of OS, with results anticipated in early 2022. We plan to present the detailed trial results at a future medical meeting, and following discussions with the FDA, we intend to submit a supplemental New Drug Application (sNDA) for the combination regimen for patients with previously untreated advanced HCC in early 2022 when the final OS data are available.

Pipeline Activities

Our small molecule discovery programs are supported by a robust and expanding infrastructure, including a library of 4.6 million compounds. We have extensive experience in the identification and optimization of drug candidates against multiple target classes for oncology, inflammation and metabolic diseases. The first compound to advance from our recent drug discovery efforts is XL092, a next-generation oral tyrosine kinase inhibitor that targets VEGF receptors, MET, AXL, MER and other kinases implicated in cancer’s growth and spread. In designing XL092, we sought to build upon our experience with cabozantinib, retaining the target profile of cabozantinib while improving key characteristics, including the pharmacokinetic half-life. To date, we have announced two large phase 1b clinical trials studying XL092, STELLAR-001 and STELLAR-002. STELLAR-001 is a phase 1b clinical trial evaluating XL092, both as a monotherapy and in combination with either atezolizumab or avelumab, an ICI developed by Merck KGaA, Darmstadt, Germany and Pfizer Inc., which is currently enrolling patients with advanced solid tumors. We expect the trial will begin to enroll expansion cohorts for patients with clear cell and non-clear cell RCC, colorectal cancer (CRC), hormone-receptor positive breast cancer, mCRPC and urothelial carcinoma (UC) in the fourth quarter of 2021. STELLAR-002 is a phase 1b clinical trial that will evaluate XL092 in combination with either nivolumab, nivolumab and ipilimumab, or nivolumab and bempegaldesleukin, an investigational CD122-preferential IL-2–pathway agonist developed by Nektar Therapeutics (Nektar). We expect to initiate dose-escalation cohorts for STELLAR-002 in the fourth quarter of 2021, and depending on the dose-escalation results, STELLAR-002 may enroll expansion cohorts for patients with clear cell and non-clear cell RCC, mCRPC and UC. To better understand the individual contribution of the therapies, treatment arms in the expansion cohorts may include XL092 as a single-agent, XL092 in combination with nivolumab, XL092 in combination with nivolumab and ipilimumab, and XL092 in combination with nivolumab and bempegaldesleukin.

We augment our small molecule discovery activities through research collaborations and in-licensing arrangements with other companies. The most advanced compound to emerge from these arrangements is XL102 (formerly AUR102), the lead program targeting cyclin-dependent kinase 7 under our collaboration with Aurigene Discovery Technologies Limited (Aurigene). Based on encouraging preclinical data, we exercised our exclusive option to license XL102 from Aurigene, and subsequently initiated a phase 1 clinical trial evaluating the compound in January 2021. In addition, we exercised our exclusive option to in-license XL114 (formerly AUR104), Aurigene’s novel anti-cancer compound that inhibits the CARD11-BCL10-MALT1 (CBM) signaling pathway, which promotes lymphocyte survival and proliferation. Following the FDA’s acceptance of our Investigational New Drug (IND) application for the small molecule in October 2021, we plan to initiate a phase 1 clinical trial evaluating XL114 as a monotherapy in patients with non-Hodgkin’s lymphoma (NHL). In furtherance of efforts to expand our portfolio of differentiated small molecule therapies, in October 2021, we entered into an exclusive collaboration and license agreement with STORM Therapeutics LTD (STORM), focused on the discovery and development of inhibitors of novel RNA modifying enzymes, including ADAR1.

Beyond small molecules, we have also launched rigorous efforts to discover and advance biologic drug candidates, such as bispecific antibodies, antibody drug conjugates (ADCs) and other innovative biologics that have the potential to become anti-cancer therapies. ADCs in particular present a unique opportunity for new cancer treatments, given their capabilities to deliver anti-cancer payload drugs to targets with increased precision while minimizing impact on healthy tissues, and have been validated by the multiple regulatory approvals for the commercial sale of ADCs. To facilitate the growth of these biologics programs, we have established multiple research collaborations and in-licensing arrangements, expanding our access to antibodies or other binders, which are the starting point for use with additional technology platforms that we employ to generate next-generation ADCs or bispecific antibodies. We have made significant progress under these arrangements and believe we will continue to do so. For example, based on promising preclinical data for XB002 (formerly known as ICON-2), the lead Tissue Factor ADC program under our research collaboration with Iconic Therapeutics, Inc. (Iconic), we exercised our exclusive option to license XB002 in December 2020. Following the FDA’s acceptance of our IND for XB002 in April 2021, we initiated a phase 1 clinical trial in June 2021. We have expanded our access to antibodies through arrangements with WuXi Biologics Ireland Limited (WuXi Bio), focused on leveraging WuXi Bio’s panel of monoclonal antibodies against an undisclosed target for the development of ADC, bispecific and certain other novel tumor-targeting biologics, and through the execution of an asset purchase agreement with GamaMabs Pharma SA (GamaMabs), under which we will, upon the closing of the asset purchase and subject to certain conditions, acquire all rights, title and interest in GamaMabs' antibody program directed at anti-Müllerian hormone receptor 2 (AMHR2), a novel oncology target with relevance in multiple forms of cancer. These antibodies, as well as those originating from collaboration with Invenra, Inc. (Invenra), which was expanded in August 2021 to include an additional 20 oncology targets, provide starting points for the construction of ADCs through our collaborations with NBE-Therapeutics AG and Catalent, Inc.'s wholly owned subsidiaries Redwood Bioscience, Inc., R.P. Scherer Technologies, LLC and Catalent Pharma Solutions, Inc., utilizing their site-specific conjugation technologies and payloads. In addition, our collaboration with Adagene Inc. (Adagene), focused on using Adagene's SAFEbody™ technology to develop novel masked ADCs or other innovative biologics, provides potential for developing ADCs or other biologics with improved therapeutic index.

We will continue to engage in business development initiatives aimed at acquiring and in-licensing promising oncology platforms and assets and then further characterize and develop them utilizing our established preclinical and clinical development infrastructure. In total, we are advancing drug candidates across approximately 25 ongoing discovery programs toward and through preclinical development.

COVID-19 Update

As of the date of this Quarterly Report on Form 10-Q, the COVID-19 pandemic continues to have a modest impact on our business operations, in particular with respect to our clinical trial and commercial activities. We have and continue to undertake considerable efforts to mitigate the various problems presented by this crisis, including as described below:

Clinical Trials. To varying degrees and at different rates across our global clinical trials, we experienced declines in screening and enrollment activity during the early days of the COVID-19 pandemic, as well as delays in new site activations and restrictions on the access to treatment sites that is necessary to monitor clinical study progress and administration. Beginning during the second quarter of 2020 and since that time, however, that trend reversed, and screening and enrollment activity began to increase. As a result, we and our collaboration partners, including principal investigators and personnel at clinical trial sites, have been successful overall in preventing material delays to our ongoing and planned clinical trials due to the COVID-19 pandemic. We have done this through ongoing assessment of the COVID-19 pandemic's impact and, wherever possible, taking proactive steps in compliance with guidance issued by the FDA, EMA and other regulatory agencies to support the safety of our patients and their access to treatment, as well as to maintain the high quality of our clinical trials. We recognize, however, that we may have to make further operational adjustments to our ongoing and planned clinical trials and that patient enrollment, and new clinical trial site initiations may again be slowed due to recurring COVID-19 outbreaks and potential reintroduction of certain restrictions intended to mitigate the spread of COVID-19.

Drug Discovery and Preclinical Development. We have fully resumed drug discovery in our laboratories following a temporary suspension of these activities while we observed the shelter in place orders issued by the State of California and Alameda County. While this temporary suspension combined with interruptions in the portion of drug discovery work outsourced to third-party contractors in regions first impacted by COVID-19 caused us to experience modest delays in the advancement of certain of our early-stage programs, we continued to substantially progress our product pipeline despite the COVID-19 pandemic, including the submission of INDs for XL102, XB002 and XL114.

Commercial Activities. Despite the challenges posed by the COVID-19 pandemic, including requiring us to temporarily shift to telephonic and virtual interactions with healthcare professionals, we believe our commercial business was only modestly impacted. Our field employees have now partially resumed their in-person promotional activities while supplementing these activities with telephonic and virtual interactions and we believe they are well-positioned to execute on our commercial objectives.

Supply Chain. We have not experienced production delays or seen any significant impairment to our supply chain as a result of the COVID-19 pandemic. In addition, we continue to maintain sufficient safety stock inventories for our commercial drug substance and drug products, which should be sufficient to maintain robust long-term supply. We continue to work closely with our third-party contract manufacturers, distributors, suppliers, comparator drug sourcing vendors and collaboration partners to safeguard both the timely production and delivery of our products.

General Business Operations. We have taken numerous precautions, some temporary and others still in place, to help mitigate the risk of transmission of the virus in the workplace, including: initially reducing the number of our employees working on-site at our Alameda headquarters; implementing a vaccination mandate and maintaining enhanced safety and social distancing protocols for those employees who have returned to working on-site, as well as initiating an on-site COVID-19 testing program and limiting certain non-essential business travel for our employees. While most of our employees worked remotely during much of 2020 and early 2021, our Alameda-based workforce has largely returned to working on-site at our headquarters consistent with the policies in place prior to the COVID-19 pandemic. As of the date of this Quarterly Report on Form 10-Q, the COVID-19 pandemic has only had a modest impact on our productivity and has not caused significant interruptions in our general business operations.

The circumstances and public health requirements surrounding the COVID-19 pandemic continue to be subject to rapid change, and we will continue to monitor new developments that could pose additional risks for us, including the spread of the Delta variant in the U.S. and other countries and the potential emergence of other SARS-CoV-2 variants that may prove especially contagious or virulent. Despite our mitigation efforts, we may experience delays or an inability to execute on our clinical and preclinical development plans, reduced revenues or other adverse impacts to our business, which are described in more detail in “Risk Factors” in Part II, Item 1A of this Quarterly Report on Form 10-Q. We recognize that this pandemic will continue to present unique challenges for us throughout the remainder of 2021, and potentially into 2022.

Third Quarter 2021 Business Updates and Financial Highlights

During the third quarter of 2021, we continued to execute on our business objectives, generating significant revenues from operations and enabling us to continue to seek to maximize the clinical and commercial potential of our products and expand our product pipeline. Significant business updates and financial highlights for the quarter and subsequent to quarter-end include:

Business Updates

- In August 2021, we announced the expansion of our collaboration with Invenra to include an additional 20 targets for multi-specific antibody, ADC and other biologic candidate discovery and development.
- In August 2021, Takeda and Ono received regulatory approval from the Japanese MHLW to manufacture and market CABOMETYX in combination with OPDIVO as a treatment for unresectable or metastatic RCC.
- In September 2021, the FDA approved CABOMETYX for the treatment of adult and pediatric patients 12 and older with locally advanced or metastatic DTC that has progressed following prior VEGF receptor-targeted therapy and who are RAI-refractory or ineligible, and we commenced the commercial launch of CABOMETYX in this indication upon such approval. The approval was based on positive results from the phase 3 pivotal trial, COSMIC-311, in which CABOMETYX met is primary endpoint of demonstrating significant improvement in PFS.
- In September 2021, cabozantinib was the subject of multiple data presentations at the ESMO 2021 Congress, which included: (i) a post-hoc exploratory analysis of CheckMate -9ER demonstrating that efficacy benefits of the combination compared with sunitinib were observed in patients regardless of their prior nephrectomy status; (ii) detailed results from the expanded Cohort 6 of COSMIC-021, demonstrating a median PFS per Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1 of 5.6 months and 6.8 months for high-risk mCRPC patients per investigator assessment and BIRC assessment, respectively; and (iii) detailed results from COSMIC-311 evaluating cabozantinib in patients with RAI-refractory DTC.
- In October 2021, we announced an exclusive collaboration and license agreement with STORM to discover and develop inhibitors of novel RNA modifying enzymes, including ADAR1.
- In October 2021, we and Aurigene announced that we exercised our exclusive option for XL114, Aurigene’s novel anti-cancer compound that inhibits the CBM signaling pathway, resulting in our assuming responsibility for all subsequent clinical development, manufacturing and commercialization of XL114. Following the FDA’s acceptance of the IND for XL114 in October 2021, we plan to initiate a phase 1 clinical trial evaluating XL114 as a monotherapy in patients with NHL.

Financial Highlights

- Net product revenues for the third quarter of 2021 were $263.1 million, compared to $168.6 million for the third quarter of 2020.
- Total revenues for the third quarter of 2021 were $328.4 million, compared to $231.1 million for the third quarter of 2020.
- Research and development expenses for the third quarter of 2021 were $163.4 million, compared to $176.8 million for the third quarter of 2020.

- Selling, general and administrative expenses for the third quarter of 2021 were $101.6 million, compared to $88.2 million for the third quarter of 2020.
- Provision for (benefit from) income taxes for the third quarter of 2021 was $15.1 million, compared to $(6.0) million for the third quarter of 2020.
- Net income for the third quarter of 2021 was $38.2 million, or $0.12 per share, basic and diluted, compared to net loss of $(32.0) million, or $(0.10) per share, basic and diluted share, for the third quarter of 2020.
- Cash, cash equivalents, restricted cash equivalents and investments were $1.8 billion as of September 30, 2021, compared to $1.5 billion as of December 31, 2020.

See *"Results of Operations"* below for a discussion of the detailed components and analysis of the amounts above.

Challenges and Risks

In addition to the challenges and risks imposed by the COVID-19 pandemic and described under "—COVID-19 Update" above, we will also continue to face challenges and risks that may impact our ability to execute on our 2021 business objectives, and some of these risks to our business have been or may be exacerbated by the COVID-19 pandemic. In particular, for the foreseeable future, we expect our ability to generate sufficient cash flow to fund our business operations and growth will depend upon the continued commercial success of CABOMETYX, both alone or in combination with other therapies, as a treatment for the highly competitive indications for which it is approved, and possibly for other indications for which cabozantinib has been or is currently being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from these trials. However, we cannot be certain that the clinical trials we and our collaboration partners are currently conducting, or may conduct in the future, will demonstrate adequate safety and efficacy in these additional indications to receive regulatory approval in the major commercial markets where CABOMETYX is approved. Even if we and our collaboration partners receive the required regulatory approvals to market cabozantinib for additional indications, we and our collaboration partners may not be able to commercialize CABOMETYX effectively and successfully in these additional indications. In addition, CABOMETYX will only continue to be commercially successful if private third-party and government payers continue to provide coverage and reimbursement. However, as is the case for all innovative pharmaceutical therapies, obtaining and maintaining coverage and reimbursement for CABOMETYX is becoming increasingly difficult, both within the U.S. and in foreign markets, because of growing concerns over healthcare cost containment and corresponding policy initiatives and activities aimed at limiting access to, and restricting the prices of, pharmaceuticals.

Achievement of our remaining 2021 business objectives will also depend on our ability to maintain a competitive position with respect to the shifting landscape of therapeutic strategy for the treatment of cancer, which we may not be able to do. While we have had success in adapting our development strategy for the cabozantinib franchise and other product candidates to address the expanding role of therapies that combine targeted agents with ICIs and/or with other mechanisms of action, it is uncertain whether current and future clinical trials will lead to regulatory approvals, or whether physicians will prescribe regimens containing our products instead of competing product combinations. Moreover, the complexities of this development strategy have required and are likely to continue to require collaboration with some of our competitors. In the longer term, we may eventually face competition from potential manufacturers of generic versions of our marketed products, including the proposed generic versions of CABOMETYX tablets that are the subject of Abbreviated New Drug Applications (ANDAs) submitted to the FDA by MSN Pharmaceuticals, Inc. (MSN) and by Teva Pharmaceuticals Development, Inc. and Teva Pharmaceuticals USA, Inc. (individually and collectively referred to as Teva), and the approval of either MSN's or Teva's ANDA could significantly decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations. Separately, our research and development objectives may be impeded by the challenges of scaling our organization to meet the demands of expanded drug development, unanticipated delays in clinical testing and the inherent risks and uncertainties associated with drug discovery operations, all of which may be increased as a result of the COVID-19 pandemic. In connection with efforts to expand our product pipeline, we may be unsuccessful in discovering new drug candidates or identifying appropriate candidates for in-licensing or acquisition.

Some of these challenges and risks are specific to our business, and others are common to companies in the biotechnology, biopharmaceutical and pharmaceutical industries with development and commercial operations. As described under "—COVID-19 Update" above, these risks have been or may be exacerbated by the COVID-19 pandemic. For a more detailed discussion of challenges and risks we face, including those relating to the COVID-19 pandemic, see "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Fiscal Year Convention

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2021, which is a 52-week fiscal year, will end on December 31, 2021 and fiscal year 2020, which was a 52-week fiscal year, ended on January 1, 2021. For convenience, references in this report as of and for the fiscal periods ended October 1, 2021 and October 2, 2020, and as of and for the fiscal year ended January 1, 2021 are indicated as being as of and for the fiscal periods ended September 30, 2021 and September 30, 2020, and the year ended December 31, 2020, respectively.

Results of Operations

Revenues

Revenues by category were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Net product revenues	$ 263,117	$ 168,587	56 %	$ 774,577	$ 541,197	43 %
License revenues	49,694	33,205	50 %	116,862	113,318	3 %
Collaboration services revenues	15,612	29,300	-47 %	92,391	62,971	47 %
Total revenues	$ 328,423	$ 231,092	42 %	$ 983,830	$ 717,486	37 %

Net Product Revenues

Gross product revenues, discounts and allowances, and net product revenues were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Gross product revenues	$ 357,462	$ 220,401	62 %	$ 1,051,871	$ 702,865	50 %
Discounts and allowances	(94,345)	(51,814)	82 %	(277,294)	(161,668)	72 %
Net product revenues	$ 263,117	$ 168,587	56 %	$ 774,577	$ 541,197	43 %

Net product revenues by product were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
CABOMETYX	$ 259,791	$ 159,555	63 %	$ 759,000	$ 522,381	45 %
COMETRIQ	3,326	9,032	-63 %	15,577	18,816	-17 %
Net product revenues	$ 263,117	$ 168,587	56 %	$ 774,577	$ 541,197	43 %

The increases in net product revenues for CABOMETYX for the three and nine months ended September 30, 2021, relative to the corresponding prior year periods, were primarily related to the increases in the number of units sold that was driven by the strong uptake for the combination therapy of CABOMETYX and OPDIVO following approval by the FDA in January 2021. The decreases in net product revenues for COMETRIQ for the three and nine months ended September 30, 2021, relative to the corresponding prior year periods, were due to the decreases in the number of COMETRIQ units sold.

We project our net product revenues for the remainder of 2021 may increase relative to the corresponding prior year period, primarily as a result of the increase in demand for CABOMETYX following the FDA's approval of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC, and to a lesser extent, an increase in selling price for CABOMETYX.

We recognize product revenues net of discounts and allowances that are described in “Note 1. Organization and Summary of Significant Accounting Policies” to our “Notes to Consolidated Financial Statements” included in our Annual Report on Form 10-K for the year ended December 31, 2020. The increase in discounts and allowances for the three months ended September 30, 2021, relative to the corresponding prior year period, was primarily the result of an increase in Public Health Service hospital utilization and the dollar amount of the related chargebacks. The increase in discounts and allowances for the nine months ended September 30, 2021, relative to the corresponding prior year period, was primarily the result of an increase in Public Health Service hospital utilization and the dollar amount of the related chargebacks and, to a lesser extent, an increase in Medicaid utilization and the dollar amount of related Medicaid rebates.

We project our discounts and allowances as a percentage of gross revenues may increase during the remainder of 2021 relative to the corresponding prior year period as the number of patients participating in government programs continues to increase and as the discounts given and rebates paid to government payers also increase.

License Revenues

License revenues include: (a) the recognition of the portion of milestone payments allocated to the transfer of intellectual property licenses for which it had become probable in the related period that the milestone would be achieved and a significant reversal of revenues would not occur; (b) royalty revenues; and (c) the profit on the U.S. commercialization of COTELLIC from Genentech.

Milestone revenues, which are allocated between license revenues and collaboration services revenues, were $19.7 million and $33.1 million for the three and nine months ended September 30, 2021, respectively, as compared to $13.5 million and $57.1 million for the corresponding prior year periods. Milestone revenues by period included the following:

- Milestone revenues for the three and nine months ended September 30, 2021 included $18.8 million in connection with a $20.0 million milestone we achieved following Takeda’s first commercial sale in Japan of CABOMETYX in combination with OPDIVO for the treatment of patients with unresectable or metastatic RCC.
- Milestone revenues for the nine months ended September 30, 2021 also included $11.9 million in connection with a $12.5 million regulatory milestone we determined, in the second quarter of 2021, was probable of achievement. The milestone was achieved in the third quarter of 2021 upon Ipsen’s submission of a variation application to the EMA for CABOMETYX as a treatment for patients with previously treated, RAI-refractory DTC.
- Milestone revenues for the three and nine months ended September 30, 2020 included $9.2 million in connection with a $10.0 million milestone related to Takeda’s and Ono’s submission of a supplemental application to the Japanese MHLW for Manufacturing and Marketing Approval of CABOMETYX in combination with OPDIVO for the treatment of patients with unresectable, advanced or metastatic RCC.
- Milestone revenues for the nine months ended September 30, 2020 also included $25.3 million in connection with $31.0 million in milestones we achieved following Takeda’s first commercial sale of CABOMETYX for the treatment of patients with curatively unresectable or metastatic RCC in Japan and $18.9 million in revenues recognized in connection with a $20.0 million development milestone from Ipsen upon the initiation of a phase 3 pivotal trial.

Royalty revenues increased primarily as a result of increases in Ipsen’s net sales of cabozantinib outside of the U.S. and Japan. Ipsen royalties were $25.1 million and $70.4 million for the three and nine months ended September 30, 2021, respectively, as compared to $19.9 million and $54.1 million for the corresponding prior year periods. Ipsen’s net sales of cabozantinib have continued to grow since their first commercial sale of the product in the fourth quarter of 2016, primarily due to increased demand of CABOMETYX, which, as of September 30, 2021, is approved in 61 countries outside of the U.S. Royalty revenues for the three and nine months ended September 30, 2021 also included $2.0 million and $5.4 million, respectively, as compared to $0.7 million and $1.0 million for the corresponding prior year periods, related to Takeda’s net sales of CABOMETYX following approval in Japan during the second quarter of 2020 for the treatment of patients with curatively unresectable or metastatic RCC.

Our share of profits on the U.S. commercialization of COTELLIC under our collaboration agreement with Genentech was $1.7 million and $5.7 million for the three and nine months ended September 30, 2021, respectively, as compared to $1.6 million and $4.4 million for the corresponding prior year periods. We also earned royalties on ex-U.S. net sales of COTELLIC by Genentech of $1.6 million and $3.3 million for the three and nine months ended September 30, 2021, respectively, as compared to $1.4 million and $3.8 million for the corresponding prior year periods.

Due to uncertainties surrounding the timing and achievement of regulatory and development milestones, it is difficult to predict future milestone revenues and milestones can vary significantly from period to period.

Collaboration Services Revenues

Collaboration services revenues include the recognition of deferred revenues for the portion of upfront and milestone payments that have been allocated to research and development services performance obligations, development cost reimbursements earned under our collaboration agreements, and product supply revenues, which are net of product supply costs and the royalties we pay on sales by Ipsen and Takeda of products containing cabozantinib. We received notification that, effective January 1, 2021, Royalty Pharma plc acquired from GlaxoSmithKline (GSK) all rights, title and interest in royalties on net product sales containing cabozantinib for non-U.S. markets for the full term of the royalty and for the U.S. market through September 2026, after which time U.S. royalties will revert back to GSK.

Development cost reimbursements were $17.5 million and $98.4 million for the three and nine months ended September 30, 2021, respectively, as compared to $26.3 million and $60.3 million for the corresponding prior year periods. The decrease in development cost reimbursements for the three months ended September 30, 2021 relative to the corresponding prior year period is primarily attributable to a decrease in spending on the COSMIC-312, CONTACT-02 and COSMIC-021 studies, as well as the impact of Takeda's decision to opt in and co-fund CONTACT-02 development costs and additional cohorts of COSMIC-021 studies in the third quarter of 2020. The increase in development cost reimbursement for the nine months ended September 30, 2021 relative to the corresponding prior year period was primarily attributable to Ipsen's decision to opt in and co-fund COSMIC-311 development costs in the second quarter of 2021. Ipsen is now responsible for 35% of the global development costs of COSMIC-311 and is obligated to reimburse us for these costs, as well as an additional payment calculated as a percentage of COSMIC-311 development costs, triggered by the timing of the exercise of its option. Accordingly, collaboration services revenues for the nine months ended September 30, 2021, includes a cumulative catch-up recognized in the second quarter of 2021 for Ipsen's share of global development costs incurred since the beginning of the study and through the end of the period. The increase in development cost reimbursements for the nine months ended September 30, 2021 was partially offset by a decrease in total spending on the COSMIC-312 and COSMIC-021 studies.

Collaboration services revenues were reduced by $3.7 million and $10.5 million for the 3% royalty we are required to pay on the net sales by Ipsen and Takeda of any product incorporating cabozantinib for the three and nine months ended September 30, 2021, respectively, as compared to $2.9 million and $7.6 million for the corresponding prior year periods. As royalty generating sales of cabozantinib by Ipsen and Takeda have increased as described above, our royalty payments have also increased.

We project our collaboration services revenues may increase for the remainder of 2021, relative to the corresponding prior year period, primarily as a result of increased development cost reimbursements related to Ipsen's opt in and co-funding of COSMIC-311 as well as projections related to our other collaboration arrangements**.**

Cost of Goods Sold

The cost of goods sold and our gross margin were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Cost of goods sold	$ 11,874	$ 8,725	36 %	$ 39,956	$ 27,235	47 %
Gross margin	95 %	95 %		95 %	95 %	

Cost of goods sold is related to our product revenues and consists primarily of a 3% royalty payable on U.S. net sales of any product incorporating cabozantinib, as well as the cost of inventory sold, indirect labor costs, write-downs related to expiring, excess and obsolete inventory, and other third-party logistics costs. The increases in cost of goods sold for the three and nine months ended September 30, 2021, relative to the corresponding prior year periods, were primarily the result of increases in royalties as a result of increased U.S. CABOMETYX sales and certain other period costs. We do not project our gross margin to change significantly during the remainder of 2021.

Research and Development Expenses

We do not track fully burdened research and development expenses on a project-by-project basis. We group our research and development expenses into three categories: (1) development; (2) drug discovery; and (3) other. Our development group leads the development and implementation of our clinical and regulatory strategies and prioritizes disease indications in which our compounds are being or may be studied in clinical trials. Our drug discovery group utilizes a variety of technologies, including in-licensed technologies, to enable the rapid discovery, optimization and extensive characterization of lead compounds and biologics such that we are able to select development candidates with the best potential for further evaluation and advancement into clinical development.

Research and development expenses by category were as follows (in thousands):

	Three Months Ended September 30,		Percent	Nine Months Ended September 30,		Percent
	2021	2020	Change	2021	2020	Change
Research and development expenses:						
Development:						
Clinical trial costs	$ 55,376	$ 72,232	-23 %	$ 165,635	$ 188,182	-12 %
Personnel expenses	26,918	21,388	26 %	84,977	62,286	36 %
Consulting and outside services	6,772	4,852	40 %	18,707	11,907	57 %
Other development costs [(1)]	18,690	5,836	220 %	33,508	15,771	112 %
Total development	$ 107,756	$ 104,308	3 %	302,827	278,146	9 %
Drug discovery:						
License and other collaboration costs	21,387	45,761	-53 %	73,291	58,013	26 %
Other drug discovery [(2)]	13,067	7,703	70 %	36,078	20,844	73 %
Total drug discovery	34,454	53,464	-36 %	109,369	78,857	39 %
Other [(3)]	21,160	18,990	11 %	59,252	36,569	62 %
Total research and development expenses	$ 163,370	$ 176,762	-8 %	$ 471,448	$ 393,572	20 %

(1) Primarily includes development milestone expense related to our in-licensing collaboration agreements as well as other miscellaneous development costs. During the three and nine months ended September 30, 2021, we recognized a $12.5 million development milestone we deemed probable of achievement under certain of our in-licensing collaboration arrangements.

(2) Primarily includes personnel expenses, consulting and outside services and laboratory supplies.

(3) Includes stock-based compensation, the allocation of general corporate costs to research and development, and development cost reimbursements in connection with our collaboration arrangement with Roche executed in December 2019.

The decrease in research and development expenses for the three months ended September 30, 2021, relative to the corresponding prior year period, was primarily related to decreases in clinical trial costs, license and other collaboration costs and stock-based compensation, partially offset by an increase in personnel expenses and other development costs. Clinical trial costs, which include services performed by third-party contract research organizations and other vendors who support our clinical trials, decreased relative to the corresponding prior year period primarily due to lower costs associated with the COSMIC-312, CONTACT-02 and COSMIC-021 studies. License and other collaboration costs decreased relative to the corresponding prior year period primarily due to decreases in upfront license fees and program initiation fees related to business development activities. Other development costs increased relative to the corresponding prior year period primarily related to a development milestone we deemed probable of achievement under certain of our in-licensing collaboration arrangements. Stock-based compensation expense decreased relative to the corresponding prior year period due to higher expense related to performance-based restricted stock units (PSUs) granted in 2019 that became probable of achievement in the third quarter of 2020, compared to the PSUs granted in 2020 that were either achieved or became probable of achievement in the third quarter of 2021. Personnel expenses increased primarily due to an increase in headcount to support our expanding discovery and development organization.

The increase in research and development expenses for the nine months ended September 30, 2021, relative to the corresponding prior year period, was primarily related to increases in personnel expenses, license and other collaboration costs, other development costs, and stock-based compensation, partially offset by a decrease in clinical trial costs. Personnel expenses increased relative to the corresponding prior year period primarily due to an increase in headcount to support our expanding discovery and development organization. License and other collaboration costs increased relative to the corresponding prior year period primarily due to increases in upfront license fees, program initiation fees, development milestones and research funding commitments related to business development activities. Other development costs increased relative to the corresponding prior year period primarily related to a development milestone we deemed probable of achievement under certain of our in-licensing collaboration arrangements. Stock-based compensation expense increased relative to the corresponding prior year period primarily due to an increase in stock-based compensation expense for service-based RSUs associated with higher headcount, partially offset by a lower stock-based compensation expense associated with PSUs. Clinical trial costs decreased relative to the corresponding prior year period primarily due to lower costs associated with the COSMIC-312 and COSMIC-021 studies.

In addition to reviewing the three categories of research and development expenses described above, we principally consider qualitative factors in making decisions regarding our research and development programs. These factors include enrollment in clinical trials for our drug candidates, preliminary data and final results from clinical trials, the potential indications for our drug candidates, the clinical and commercial potential for our drug candidates, and competitive dynamics. We also make our research and development decisions in the context of our overall business strategy.

We are focusing a significant amount of our development efforts on cabozantinib to maximize the therapeutic and commercial potential of this compound and, as a result, we project that a substantial portion of our research and development expenses will relate to the continuing clinical development program of cabozantinib, which includes over 100 ongoing or planned clinical trials across multiple indications. Notable ongoing company-sponsored studies resulting from this program include: COSMIC-313, for which BMS is providing nivolumab and ipilimumab free of charge and CONTACT-02 for which Roche is sharing the development costs and providing atezolizumab free of charge.

We are expanding our oncology product pipeline through drug discovery efforts, which encompass both small molecule and biologics programs with multiple modalities and mechanisms of action. In this regard, we conduct drug discovery activities with the goal of identifying new product candidates to advance into clinical trials. In addition, we will continue to engage in business development initiatives aimed at acquiring and in-licensing promising oncology platforms and assets and then further characterize and develop them utilizing our established preclinical and clinical development infrastructure.

We project our research and development expenses may increase for the remainder of 2021, relative to the corresponding prior year period, primarily driven by our ongoing clinical evaluation of cabozantinib, the initiation of new clinical trials and expansion of ongoing clinical trials evaluating other product candidates in our pipeline, including current early-stage trials evaluating XL092, XL102, XB002 and anticipated business development activities.

The length of time required for clinical development of a particular product candidate and our development costs for that product candidate may be impacted by the scope and timing of enrollment in clinical trials for the product candidate, our decisions to develop a product candidate for additional indications and whether we pursue development of the product candidate or a particular indication with a collaborator or independently. For example, cabozantinib is being developed in multiple indications, and we do not yet know for how many of those indications we will ultimately pursue regulatory approval. In this regard, our decisions to pursue regulatory approval of cabozantinib for additional indications depend on several variables outside of our control, including the strength of the data generated in our prior, ongoing and potential future clinical trials. Furthermore, the scope and number of clinical trials required to obtain regulatory approval for each pursued indication is subject to the input of the applicable regulatory authorities, and we have not yet sought such input for all potential indications that we may elect to pursue. Even after having given such input, applicable regulatory authorities may subsequently require additional clinical studies prior to granting regulatory approval based on new data generated by us or other companies, or for other reasons outside of our control. As a condition to any regulatory approval, we may also be subject to post-marketing development commitments, including additional clinical trial requirements. As a result of the uncertainties discussed above, we are unable to determine the duration of, or total costs associated with the development of cabozantinib or any of our other research and development projects.

Our potential therapeutic products are subject to a lengthy and uncertain regulatory process that may not result in our receipt of the necessary regulatory approvals. Failure to receive the necessary regulatory approvals would prevent us from commercializing the product candidates affected, including cabozantinib in any additional indications. In addition, clinical trials of our potential product candidates may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval. A discussion of the risks and uncertainties with respect to our research and development activities and the consequences to our business, financial position and growth prospects can be found in “Risk Factors” in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Selling, general and administrative expenses	$ 101,558	$ 88,185	15 %	$ 302,404	$ 210,916	43 %

Selling, general and administrative expenses consist primarily of personnel expenses, stock-based compensation, marketing costs and certain other administrative costs.

The increases in selling, general and administrative expenses for the three and nine months ended September 30, 2021, relative to the corresponding prior year periods, were primarily related to increases in personnel expenses, corporate giving and marketing costs. In the three months ended September 30, 2021, the increase in selling, general and administrative expenses was partially offset by a decrease in stock-based compensation expense. Personnel expenses increased relative to the corresponding prior year periods primarily due to increases in administrative headcount to support our commercial and research and development organizations. Marketing costs increased relative to the corresponding prior year period primarily due to increased marketing activities in support of the launch of the combination therapy of CABOMETYX and OPDIVO for the treatment of advanced RCC following approval by the FDA in January 2021. The decrease in stock-based compensation expense for the three months ended September 30, 2021 relative to the corresponding prior year period was primarily due to higher compensation expense associated with the PSUs granted in 2019 that became probable of achievement in the third quarter of 2020 compared to the PSUs granted in 2020 that were either achieved or became probable of achievement in the third quarter of 2021.

We project our selling, general and administrative expenses may continue to increase for the remainder of 2021 relative to the corresponding prior year period in support of our continued commercial investment in CABOMETYX and the growth in the broader organization.

Non-operating Income

Non-operating income was as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Interest income	$ 1,658	$ 3,994	-58 %	$ 6,231	$ 16,376	-62 %
Other income (expense), net	(19)	565	n/a	(120)	571	n/a
Non-operating income	$ 1,639	$ 4,559	-64 %	$ 6,111	$ 16,947	-64 %

The decreases in non-operating income for the three and nine months ended September 30, 2021, relative to the corresponding prior year periods, were primarily the result of the decreases in interest income due to lower interest rates.

Provision for (Benefit From) Income Taxes

The provision for (benefit from) income taxes and effective income tax rates were as follows (dollars in thousands):

	Three Months Ended September 30,		Percent Change	Nine Months Ended September 30,		Percent Change
	2021	2020		2021	2020	
Provision for (benefit from) income taxes	$ 15,056	$ (5,981)	n/a	$ 40,236	$ 19,317	108 %
Effective tax rate	28.3 %	15.7 %		22.8 %	18.8 %	

We recorded an income tax provision for the three months ended September 30, 2021 as a result of our current period reported pre-tax income, as compared to the corresponding prior year period, in which we recorded a benefit from income taxes as a result of a reported pre-tax loss. The increase in provision for income taxes for the nine months ended September 30, 2021, as compared to the corresponding prior year period, was due to the increase in pre-tax income. The effective tax rate for the three and nine months ended September 30, 2021 differed from the U.S. federal statutory rate of

21% primarily due to non-deductible executive compensation, partially offset by excess tax benefits related to the exercise of certain stock options during the periods and the generation of federal tax credits. The effective tax rate for the three and nine months ended September 30, 2020 differed from the U.S. federal statutory rate of 21% primarily due to excess tax benefits related to the exercise of certain stock options, the generation of federal tax credits, partially offset by non-deductible executive compensation during the periods.

Liquidity and Capital Resources

As of September 30, 2021, we had $1.8 billion in cash, cash equivalents, restricted cash equivalents and investments, compared to $1.5 billion as of December 31, 2020. We anticipate that the aggregate of our current cash and cash equivalents, short-term investments available for operations, net product revenues and collaboration revenues will enable us to maintain our operations for a period of at least 12 months following the filing date of this report.

We project we may continue to spend significant amounts of cash to fund the continued development and commercialization of cabozantinib. In addition, we intend to continue to expand our oncology product pipeline through our drug discovery efforts, including additional research collaborations, in-licensing arrangements and other business development activities that align with our oncology drug development, regulatory and commercial expertise. Financing these activities could materially impact our liquidity and capital resources and may require us to incur debt or raise additional funds through the issuance of equity. Furthermore, even though we believe we have sufficient funds for our current and future operating plans, we may choose to incur debt or raise additional funds through the issuance of equity due to market conditions or strategic considerations.

Letters of Credit

We have obtained standby letters of credit related to our lease obligations and certain other obligations with combined credit limits of $31.2 million and $1.6 million as of September 30, 2021 and December 31, 2020, respectively.

In January 2021, we entered into a standby letter of credit as guarantee of our obligation to fund our portion of the tenant improvements related to our build-to-suit lease at our corporate campus. The letter of credit is secured by our short-term investments, which are recorded as restricted cash equivalents and presented in other long-term assets in our Condensed Consolidated Balance Sheets and will be reduced as we fund our portion of the tenant improvements. As of September 30, 2021, restricted cash equivalents included $29.6 million of short-term investments as collateral under our standby letter of credit for our portion of the tenant improvements.

Sources and Uses of Cash

Cash flow activities were as follows (in thousands):

	Nine Months Ended September 30,	
	2021	2020
Net cash provided by operating activities	$ 304,352	$ 175,689
Net cash used in investing activities	$ (29,829)	$ (101,706)
Net cash provided by (used in) financing activities	$ 3,193	$ (6,438)

Operating Activities

Cash flows provided by operating activities represent the cash receipts and disbursements related to all of our activities other than investing and financing activities. Cash provided by operating activities is derived by adjusting our net income for: non-cash operating items such as deferred taxes, stock-based compensation, depreciation, non-cash lease expense and changes in operating assets and liabilities which reflect timing differences between the receipt and payment of cash associated with transactions and when they are recognized in our Condensed Consolidated Statements of Income (Loss).

Cash provided by operating activities for the nine months ended September 30, 2021 increased relative to the corresponding prior year period, primarily due to an increase in cash received on sales of our products, an increase in cash received from our commercial collaboration arrangements and net favorable changes in operating assets and liabilities, partially offset by an increase in cash paid for operating expenses.

Investing Activities

Cash used in investing activities for the nine months ended September 30, 2021 consisted of cash used in investment purchases of $1,077.4 million and purchases of property, equipment and other of $48.3 million, partially offset by proceeds from the maturities and sales of investments of $1,095.8 million.

Cash used in investing activities for the nine months ended September 30, 2020 consisted of cash used in investment purchases of $867.0 million and purchases of property, equipment and other of $16.1 million, partially offset by proceeds from the maturities and sales of investments of $781.3 million.

Financing Activities

Cash provided by financing activities for the nine months ended September 30, 2021 consisted of $18.2 million in proceeds from the issuance of common stock under our equity incentive and stock purchase plans, partially offset by $15.0 million of withholding taxes paid related to net share settlements of equity awards.

Cash used in financing activities for the nine months ended September 30, 2020 included $26.1 million of withholding taxes paid related to net share settlements of equity awards, partially offset by $19.7 million in proceeds from the issuance of common stock under our equity incentive and stock purchase plans.

Contractual Obligations

There were no material changes outside of the ordinary course of business in our contractual obligations as of September 30, 2021 from those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2020.

Off-Balance Sheet Arrangements

As of September 30, 2021, we did not have any material off-balance-sheet arrangements, as defined by applicable SEC regulations.

Critical Accounting Policies and Estimates

The preparation of our Condensed Consolidated Financial Statements conforms to accounting principles generally accepted in the U.S. which requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosures. An accounting policy is considered to be critical if it requires an accounting estimate to be made based on assumptions about matters that are highly uncertain at the time the estimate is made, and if different estimates that reasonably could have been used, or changes in the accounting estimates that are reasonably likely to occur periodically, could materially impact our Condensed Consolidated Financial Statements. On an ongoing basis, management evaluates its estimates including, but not limited to: those related to revenue recognition, including determining the nature and timing of satisfaction of performance obligations, and determining the standalone selling price of performance obligations, and variable consideration such as rebates, chargebacks, sales returns and sales allowances as well as milestones included in collaboration arrangements; the amounts of revenues and expenses under our profit and loss sharing agreement; recoverability of inventory; the accrual for certain liabilities including accrued clinical trial liabilities; and valuations of equity awards used to determine stock-based compensation, including certain awards with vesting subject to market or performance conditions; and the amounts of deferred tax assets and liabilities including the related valuation allowance. We base our estimates on historical experience and on various other market-specific and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our senior management has discussed the development, selection and disclosure of these estimates with the Audit Committee of our Board of Directors. Actual results could differ materially from those estimates.

We believe our critical accounting policies relating to revenue recognition, inventory, clinical trial accruals, stock-based compensation and income taxes reflect the most significant estimates and assumptions used in the preparation of our Condensed Consolidated Financial Statements.

There have been no significant changes in our critical accounting policies and estimates during the nine months ended September 30, 2021, as compared to the critical accounting policies and estimates disclosed in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our Annual Report on Form 10-K for the year ended December 31, 2020 submitted to the SEC on February 10, 2021.

Recent Accounting Pronouncements

For a description of the expected impact of recent accounting pronouncements, see “Note 1. Organization and Summary of Significant Accounting Policies” in the “Notes to Condensed Consolidated Financial Statements” contained in Part I, Item 1 of this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Our market risks as of September 30, 2021 have not changed significantly from those described in Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2020.

Item 4. Controls and Procedures

Evaluation of disclosure controls and procedures. Based on the evaluation of our disclosure controls and procedures (as defined in Rules 13a-15(e) or 15d-15(e) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) required by Rules 13a-15(b) or 15d-15(b) of the Exchange Act, our Chief Executive Officer and Chief Financial Officer have concluded that as of the end of the period covered by this report, our disclosure controls and procedures were effective at the reasonable assurance level.

Limitations on the effectiveness of controls. A control system, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were effective to provide reasonable assurance that the objectives of our disclosure control system were met.

Changes in internal control over financial reporting. There were no changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

In September 2019, we received a notice letter regarding an ANDA submitted to the FDA by MSN, requesting approval to market a generic version of CABOMETYX tablets. MSN's initial notice letter included a Paragraph IV certification with respect to our U.S. Patent Nos. 8,877,776, 9,724,342, 10,034,873 and 10,039,757, which are listed in the Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book, for CABOMETYX. MSN's initial notice letter did not provide a Paragraph IV certification against U.S. Patent No. 7,579,473, the composition of matter patent, or U.S. Patent No. 8,497,284, a method of use patent, each of which is listed in the Orange Book. On October 29, 2019, we filed a complaint in the United States District Court for the District of Delaware (the Delaware District Court) for patent infringement against MSN asserting U.S. Patent No. 8,877,776 arising from MSN's ANDA filing with the FDA. On November 20, 2019, MSN filed its response to the complaint, alleging that U.S. Patent No. 8,877,776 is invalid and not infringed. On May 5, 2020, we received notice from MSN that it had amended its ANDA to assert additional Paragraph IV certifications. The ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of the two previously unasserted CABOMETYX patents: U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284. On May 11, 2020, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284 arising from MSN's amended ANDA filing with the FDA. Neither of our complaints alleges infringement of U.S. Patent Nos. 9,724,342, 10,034,873 and 10,039,757. On May 22, 2020, MSN filed its response to the complaint, alleging that each of U.S. Patent No. 7,579,473 and U.S. Patent No. 8,497,284 is invalid and not infringed. On March 23, 2021, MSN filed its First Amended Answer and Counterclaims (amending its prior filing from May 22, 2020), seeking, among other things, a declaratory judgment that U.S. Patent No. 9,809,549 is invalid and would not be infringed by MSN if its generic version of CABOMETYX tablets were approved by the FDA. U.S. Patent No. 9,809,549 is not listed in the Orange Book. On April 7, 2021, we filed our response to MSN's First Amended Answer and Counterclaims, denying, among other things, that U.S. Patent No. 9,809,549 is invalid or would not be infringed.

On October 1, 2021, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patent Nos. 7,579,473 and 8,497,284, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patent Nos. 7,579,473 and 8,497,284 would also infringe certain claims of each patent, if those claims are not found to be invalid. Then, on October 12, 2021, pursuant to a separate stipulation between us and MSN, the Delaware District Court entered an order dismissing MSN's counterclaims with respect to U.S. Patent No. 9,809,549. In our complaints, we are seeking, among other relief, an order that the effective date of any FDA approval of MSN's ANDA be a date no earlier than the expiration of all of U.S. Patent No. 7,579,473, U.S. Patent No. 8,497,284 and U.S. Patent No. 8,877,776, the latest of which expires on October 8, 2030, and equitable relief enjoining MSN from infringing these patents. These lawsuits against MSN have been consolidated, and a bench trial has been scheduled for May 2022.

In May 2021, we received notice letters from Teva regarding an ANDA Teva submitted to the FDA, requesting approval to market a generic version of CABOMETYX tablets. Teva's notice letters included a Paragraph IV certification with respect to our U.S. Patent Nos. 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Orange Book and expire in 2033, 2031 and 2031, respectively. Teva's notice letters did not provide a Paragraph IV certification against any additional CABOMETYX patents. On June 17, 2021, we filed a complaint in the Delaware District Court for patent infringement against Teva, along with Teva Pharmaceutical Industries Limited (Teva Parent), asserting U.S. Patent Nos. 9,724,324 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment) arising from Teva's ANDA filing with the FDA. On August 27, 2021, Teva filed its answer and counterclaims to the complaint, alleging that all of U.S. Patent Nos. 9,724,324, 10,034,873 and 10,039,757 are invalid and not infringed, and on August 23, 2021, we and Teva entered into a stipulation wherein Teva Parent was dismissed without prejudice from this lawsuit and agreed to be bound by any stipulation, judgment, order or decision rendered as to Teva, including any appeals and any order granting preliminary or permanent injunctive relief against Teva. On September 17, 2021, we filed an answer to Teva's counterclaims. We are seeking, among other relief, an order that the effective date of any FDA approval of Teva's ANDA be a date no earlier than the expiration of all of U.S. Patent Nos. 9,724,342, 10,034,873 and 10,039,757, the latest of which expires on July 9, 2033, and equitable relief enjoining Teva from infringing these patents. A bench trial has been scheduled for June 2023.

We may also from time to time become a party or subject to various other legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. Some of these proceedings have involved, and may involve in the future, claims that are subject to substantial uncertainties and unascertainable damages.

Item 1A. Risk Factors

In addition to the risks discussed elsewhere in this report, the following are important factors that make an investment in our securities speculative or risky, and that could cause actual results or events to differ materially from those contained in any forward-looking statements made by us or on our behalf. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or that we deem immaterial also may impair our business operations. If any of the following risks or such other risks actually occur, our business and the value of your investment in our company could be harmed.

Risk Factor Summary

- *Our ability to grow our company is critically dependent upon the commercial success of CABOMETYX in its approved indications and the further clinical development, regulatory approval and commercial success of the cabozantinib franchise in additional indications.*
- *If we are unable to obtain or maintain coverage and reimbursement for our products from third-party payers, our business will suffer.*
- *Pricing for pharmaceutical products in the U.S. has come under increasing attention and scrutiny by federal and state governments, legislative bodies and enforcement agencies. This may result in actions that have the effect of reducing our revenue or harming our business or reputation.*
- *Lengthy regulatory pricing and reimbursement procedures and cost control initiatives imposed by governments outside the U.S. could delay the marketing of and/or result in downward pressure on the price of our approved products, resulting in a decrease in revenue.*
- *Legislation and regulatory action designed to reduce barriers to the development, approval and adoption of generic drugs in the U.S., and the entrance of generic competitors, could limit the revenue we derive from our products, which could have a material adverse impact on our business, financial condition and results of operations.*
- *We are subject to healthcare laws, regulations and enforcement, as well as laws and regulations relating to privacy, data collection and processing of personal data; our failure to comply with those laws could have a material adverse impact on our business, financial condition and results of operations.*
- *Clinical testing of cabozantinib for new indications, or of new product candidates, is a lengthy, costly, complex and uncertain process that may fail ultimately to demonstrate safety and efficacy data for those products sufficiently differentiated to compete in our highly competitive market environment.*
- *The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy and uncertain and may not result in regulatory approvals for additional cabozantinib indications or our other product candidates, which could have a material adverse impact on our business, financial condition and results of operations.*
- *We may be unable to expand our development pipeline, which could limit our growth and revenue potential.*
- *Our profitability could be negatively impacted if expenses associated with our extensive clinical development, business development and commercialization activities, both for the cabozantinib franchise and our earlier-stage product candidates, grow more quickly than the revenues we generate.*
- *Our clinical, regulatory and commercial collaborations with major companies make us reliant on those companies for their continued performance and investments, which subjects us to a number of risks. For example, we rely on Ipsen and Takeda for the commercial success of CABOMETYX in its approved indications outside of the U.S., and we are unable to control the amount or timing of resources expended by these collaboration partners in the commercialization of CABOMETYX in its approved indications outside of the U.S. In addition, our growth potential is dependent in part upon companies with which we have entered into research collaborations, in-licensing arrangements and similar business development relationships.*
- *Data breaches, cyber-attacks and other failures in our information technology operations and infrastructure could compromise our intellectual property or other sensitive information, damage our operations and cause significant harm to our business and reputation.*
- *If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could adversely affect our ability to compete in the market.*

- *If the COVID-19 pandemic is further prolonged or becomes more severe, our business operations and corresponding financial results could suffer, which could have a material adverse impact on our financial condition and prospects for growth.*
- *The loss of key personnel or the inability to retain and, where necessary, attract additional personnel could impair our ability to operate and expand our operations.*

Risks Related to the Commercialization of Our Products

Our ability to grow our company is critically dependent upon the commercial success of CABOMETYX in its approved indications and the further clinical development, regulatory approval and commercial success of the cabozantinib franchise in additional indications.

We anticipate that for the foreseeable future, our ability to maintain or meaningfully increase cash flow to fund our business operations and growth will depend upon the continued commercial success of CABOMETYX, both alone and in combination with other therapies, as a treatment for the highly competitive indications for which it is approved, and possibly for other indications for which cabozantinib has been or is currently being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from these trials. In this regard, part of our strategy is to pursue additional indications for the cabozantinib franchise to increase the number of cancer patients who could benefit from this medicine. However, we cannot be certain that the clinical trials we and our collaboration partners are currently conducting, or may conduct in the future, will demonstrate adequate safety and efficacy in these additional indications to receive regulatory approval in the major commercial markets where CABOMETYX is approved. Even if we and our collaboration partners receive the required regulatory approvals to market cabozantinib for additional indications, we and our collaboration partners may not be able to commercialize CABOMETYX effectively and successfully in these additional indications. If revenue from CABOMETYX decreases or remains flat, or if we are unable to expand the labeled indications in major commercial markets where CABOMETYX is approved, or if we or our collaboration partners fail to achieve anticipated product royalties and collaboration milestones, whether as a result of the COVID-19 pandemic or otherwise, we may need to reduce our operating expenses, access other sources of cash or otherwise modify our business plans, which could have a material adverse impact on our business, financial condition and results of operations.

Our ability to grow revenues from sales of CABOMETYX depends upon the degree of market acceptance among physicians, patients, healthcare payers, and the medical community.

Our ability to increase or maintain revenues from sales of CABOMETYX for its approved indications is, and if approved for additional indications will be, highly dependent upon the extent of market acceptance of CABOMETYX among physicians, patients, government healthcare payers such as Medicare and Medicaid, commercial healthcare plans and the medical community. Market acceptance for CABOMETYX could be impacted by numerous factors, including the effectiveness and safety profile, or the perceived effectiveness and safety profile, of CABOMETYX compared to competing products, the strength of CABOMETYX sales and marketing efforts and changes in pricing and reimbursement for CABOMETYX. If CABOMETYX does not continue to be prescribed broadly for the treatment of patients in its approved indications, our product revenues could flatten or decrease, which could have a material adverse impact on our business, financial condition and results of operations.

Our competitors may develop products, combination therapies and technologies that impair the relative value of our marketed products and any future product candidates.

The biotechnology, biopharmaceutical and pharmaceutical industries are competitive and are characterized by constant technological change and diverse offerings of products, particularly in the area of novel oncology therapies. Many of our competitors have greater capital resources, larger research and development staff and facilities, deeper regulatory expertise and more extensive product manufacturing and commercial capabilities than we do, which may afford them a competitive advantage. Further, our competitors may be more effective at in-licensing and developing new commercial products that could render our products, and those of our collaboration partners, obsolete and noncompetitive. We face, and will continue to face, intense competition from biotechnology, biopharmaceutical and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing scientific and clinical research activities similar to ours.

Furthermore, the specific indications for which CABOMETYX is currently or may be approved, based on the results from clinical trials currently evaluating cabozantinib, are highly competitive. Several novel therapies and combinations of therapies have been approved, are in advanced stages of clinical development or are under expedited regulatory review in these indications, and these other therapies are currently competing or are expected to compete with CABOMETYX. Given the shifting landscape of therapeutic strategy following the advent of ICIs, we believe our future success will depend upon our ability to achieve positive clinical trial results for therapies combining cabozantinib with ICIs across multiple indications, and if approved, successfully commercialize such combination therapies. While we have had success in adapting our development strategy for the cabozantinib franchise to address the expanding role of therapies that combine ICIs with other targeted agents, including the FDA approval of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC, it is uncertain whether current and future clinical trials, including those evaluating cabozantinib in combination with an ICI in HCC, NSCLC and mCRPC, will lead to regulatory approvals, or whether physicians will prescribe regimens containing cabozantinib instead of competing product combinations. Moreover, the complexities of this development strategy have required and are likely to continue to require collaboration with some of our competitors.

If we are unable to maintain or increase our sales, marketing, market access and product distribution capabilities for our products, we may be unable to maximize product revenues, which could have a material adverse impact on our business, financial condition and results of operations.

Maintaining our sales, marketing, market access and product distribution capabilities requires significant resources, and there are numerous risks involved with maintaining and continuously improving such a commercial organization, including our potential inability to successfully recruit, train, retain and incentivize adequate numbers of qualified and effective sales and marketing personnel. We are competing for talent with numerous commercial- and precommercial-stage, oncology-focused biotechnology companies seeking to build out and maintain their commercial organizations, as well as other large pharmaceutical and biotechnology organizations that have extensive, well-funded and more experienced sales and marketing operations, and we may be unable to maintain or adequately scale our commercial organization as a result of such competition. Also, to the extent that the commercial opportunities for CABOMETYX grow over time, we may not properly scale the size and experience of our commercialization teams to market and sell CABOMETYX successfully in an expanded number of indications. If we are unable to maintain or scale our commercial function appropriately, or should we have to revert back to primarily telephonic and virtual interactions in lieu of in-person meetings with healthcare professionals for an extended period of time as a result of the COVID-19 pandemic, we may not be able to maximize product revenues, which could have a material adverse impact on our business, financial condition and results of operations.

If we are unable to obtain or maintain coverage and reimbursement for our products from third-party payers, our business will suffer.

Our ability to commercialize our products successfully is highly dependent on the extent to which health insurance coverage and reimbursement is, and will be, available from third-party payers, including governmental payers, such as Medicare and Medicaid, and private health insurers. Third-party payers continue to scrutinize and manage access to pharmaceutical products and services and may limit reimbursement for newly approved products and indications. Patients are generally not capable of paying for CABOMETYX or COMETRIQ themselves and rely on third-party payers to pay for, or subsidize, the costs of their medications, among other medical costs. Accordingly, market acceptance of CABOMETYX and COMETRIQ is dependent on the extent to which coverage and reimbursement is available from third-party payers. These entities could refuse, limit or condition coverage for our products, such as by using tiered reimbursement or pressing for new forms of contracting. If third-party payers do not provide coverage or reimbursement for CABOMETYX or COMETRIQ, our revenues and results of operations will suffer. In addition, even if third-party payers provide some coverage or reimbursement for CABOMETYX or COMETRIQ, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans, which often varies based on the type of contract or plan purchased, may not be sufficient for patients to afford CABOMETYX or COMETRIQ.

Current healthcare laws and regulations in the U.S. and future legislative or regulatory reforms to the U.S. healthcare system may affect our ability to commercialize our marketed products profitably.

Federal and state governments in the U.S. are considering legislative and regulatory proposals to change the U.S. healthcare system in ways that could affect our ability to continue to commercialize CABOMETYX and COMETRIQ profitably. Similarly, among policy makers and payers, there is significant interest in promoting such changes with the stated goals of containing healthcare costs, improving quality and expanding patient access. The life sciences industry and specifically the market for the sale, insurance coverage and distribution of pharmaceuticals has been a particular focus of these efforts and would likely be significantly affected by any major legislative or regulatory initiatives.

For instance, efforts to repeal, substantially modify or invalidate some or all of the provisions of the Patient Protection and Affordable Care Act of 2010, as amended (PPACA), some of which have been successful, create considerable uncertainties for all businesses involved in healthcare, including our own. Although such efforts have not significantly impacted our business to date, it is possible that the PPACA will be subject to judicial or legislative challenges in the future, which may have a material adverse impact on our business, financial condition and results of operations, and we cannot predict how future healthcare reform measures of the Biden administration and federal or state legislative or administrative changes relating to healthcare reform will affect our business.

In addition, there are pending federal and state-level legislative proposals that would significantly expand government-provided health insurance coverage, ranging from establishing a single-payer, national health insurance system to more limited “buy-in” options to existing public health insurance programs, each of which could have a significant impact on the healthcare industry. It is also possible that additional governmental actions will be taken in response to the ongoing COVID-19 pandemic, and that such actions would have a significant impact on these public health insurance programs. While we cannot predict how future legislation (or enacted legislation that has yet to be implemented) will affect our business, such proposals could have the potential to impact access to and sales of our products. Furthermore, the expansion of the 340B Drug Discount Program through the PPACA (the 340B Program) has increased the number of purchasers who are eligible for significant discounts on branded drugs, including our marketed products. Because we participate in the 340B Program to sell a portion of our marketed products, changes in the administration of the program could have a material adverse impact on our revenues, including the implementation of the program’s Administrative Dispute Resolution Process, which is in part intended to resolve claims by covered entities that manufacturers have overcharged them for covered outpatient drugs. Due to general uncertainty in the current regulatory and healthcare policy environment, and specifically regarding positions that the Biden Administration may take with respect to these issues, we are unable to predict the impact of any legislative, regulatory, third-party payer or policy actions, including potential cost containment and healthcare reform measures. If enacted, we and any third parties we may engage may be unable to adapt to any changes implemented as a result of such measures, and we may have difficulties in sustaining profitability or otherwise experience a material adverse impact on our business, financial condition and results of operations.

Pricing for pharmaceutical products in the U.S. has come under increasing attention and scrutiny by federal and state governments, legislative bodies and enforcement agencies. This may result in actions that have the effect of reducing our revenue or harming our business or reputation.

There continue to be U.S. Congressional inquiries, hearings and proposed and enacted federal legislation and rules, as well as executive orders, designed to, among other things: reduce or limit the prices of drugs and make them more affordable for patients (including, for example, by tying the prices that Medicare reimburses for physician-administered drugs to the prices of drugs in other countries); reform the structure and financing of Medicare Part D pharmaceutical benefits, including through increasing manufacturer contributions to offset Medicare beneficiary costs; bring more transparency to drug pricing rationale and methodologies; implement data collection and reporting under Section 204 of Title II of Division BB of the Consolidated Appropriations Act, 2021, which requires, among other things, health plans and issuers to disclose rebates, fees and other remuneration provided by drug manufacturers related to certain pharmaceutical products; enable the government to negotiate prices under Medicare; revise rules associated with the calculation of average manufacturer price and best price under Medicaid, which affect the amount of rebates that we pay on prescription drugs under Medicaid and to covered entities under the 340B Program; eliminate the Anti-Kickback Statute (AKS) discount safe harbor protection for manufacturer rebate arrangements with Medicare Part D plan sponsors; create new AKS safe harbors applicable to certain point-of-sale discounts to patients and fixed fee administrative fee payment arrangements with pharmacy benefit managers; and facilitate the importation of certain lower-cost drugs from other countries. For instance, President Biden issued an executive order in July 2021 supporting legislation to enact some of these drug pricing reforms, and in response, the U.S. Department of Health and Human Services (HHS) released a Comprehensive Plan for Addressing High Drug Prices in September 2021 with specific legislative and administrative policies that Congress could enact to help improve affordability of and access to prescription drugs. While we cannot know the final form or timing of any such legislative, regulatory and/or administrative measures, some of the pending and enacted legislative proposals or executive rulemaking, such as those incorporating International Pricing Index or Most-Favored-Nation models, if implemented without successful legal challenges, would likely have a significant and far-reaching impact on the biopharmaceutical industry and therefore also likely have a material adverse impact on our business, financial condition and results of operations.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, marketing cost disclosure and transparency measures, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing, including the National Medicaid Pooling Initiative. In particular, the obligation to provide notices of price increases to purchasers under laws such as California's SB-17 may influence customer ordering patterns for CABOMETYX and COMETRIQ, which in turn may increase the volatility of our revenues as a reflection of changes in inventory volumes. Furthermore, adoption of these drug pricing transparency regulations, and our associated compliance obligations, may increase our general and administrative costs and/or diminish our revenues. Implementation of these federal and/or state cost-containment measures or other healthcare reforms may limit our ability to generate product revenue or commercialize our products, and in the case of drug pricing transparency regulations, may result in fluctuations in our results of operations.

Lengthy regulatory pricing and reimbursement procedures and cost control initiatives imposed by governments outside the U.S. could delay the marketing of and/or result in downward pressure on the price of our approved products, resulting in a decrease in revenue.

Outside the U.S., including major markets in the EU and Japan, the pricing and reimbursement of prescription pharmaceuticals is generally subject to governmental control. In these countries, pricing and reimbursement negotiations with governmental authorities or payers can take six to 12 months or longer after the initial marketing authorization is granted for a product, or after the marketing authorization for a new indication is granted. This can substantially delay broad availability of the product. To obtain reimbursement and/or pricing approval in some countries, our collaboration partners Ipsen and Takeda may also be required to conduct a study or otherwise provide data that seeks to establish the cost effectiveness of CABOMETYX compared with other available established therapies. The conduct of such a study could also result in delays in the commercialization of CABOMETYX.

Additionally, cost-control initiatives, increasingly based on affordability and accessibility, as well as post-marketing assessments of the added value of CABOMETYX and COMETRIQ as compared to existing treatments, could influence the prices paid for and net revenues we realize from CABOMETYX and COMETRIQ, or the indications for which we are able to obtain reimbursement, which would result in lower license revenues to us. Upcoming legislative and policy changes in the EU, some of which may materialize during 2022, are aimed at increasing cooperation between the EU Member States. Such initiatives, particularly the Regulation on Health Technology Assessment, may further impact the price and reimbursement status of CABOMETYX and COMETRIQ in the future.

Legislation and regulatory action designed to reduce barriers to the development, approval and adoption of generic drugs in the U.S., and the entrance of generic competitors, could limit the revenue we derive from our products, which could have a material adverse impact on our business, financial condition and results of operations.

Under the Federal Food, Drug, and Cosmetic Act (FDCA), the FDA can approve an ANDA for a generic version of a branded drug without the applicant undertaking the human clinical testing necessary to obtain approval to market a new drug. The FDA can also approve a New Drug Application (NDA) under section 505(b)(2) of the FDCA that relies in part on the agency's findings of safety and/or effectiveness for a previously approved drug, where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. Both the ANDA and 505(b)(2) NDA processes are discussed in more detail in "Item 1. Business—Government Regulation—FDA Review and Approval" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020. In either case, if an ANDA or 505(b)(2) NDA applicant submits an application referencing one of our marketed products prior to the expiry of one or more our Orange Book-listed patents for the applicable product, we may litigate with the potential generic competitor to protect our patent rights, which would result in substantial costs, divert the attention of management, and could have an adverse impact on our stock price. For example, MSN and Teva have separately submitted ANDAs to the FDA requesting approval to market their respective generic versions of CABOMETYX tablets, and we have subsequently filed patent lawsuits against both companies. For a more detailed discussion of these litigation matters, see "Legal Proceedings" in Part II, Item 1 of this Quarterly Report on Form 10-Q. It is possible that MSN, Teva or other companies, following FDA approval of an ANDA or 505(b)(2) NDA, could introduce generic or otherwise competitor versions of our marketed products before our patents expire if they do not infringe our patents or if it is determined that our patents are invalid or unenforceable, and we expect that generic cabozantinib products would be offered at a significantly lower price compared to our marketed cabozantinib products. Therefore, regardless of the regulatory approach, the introduction of a generic version of cabozantinib could significantly decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations.

The U.S. federal government has also taken numerous legislative and regulatory actions to expedite the development and approval of generic drugs and biosimilars. For instance, the FDA Reauthorization Act of 2017 includes, inter alia, measures to expedite the development and approval of generic products, where generic competition is lacking even in the absence of exclusivities or listed patents. In addition, the Ensuring Innovation Act, enacted on April 23, 2021, amended the FDA's statutory authority for granting new chemical entity (NCE) exclusivity to reflect the agency's existing regulations and longstanding interpretation that award NCE exclusivity based on a drug's active moiety, as opposed to its active ingredient, which is intended to limit the applicability of NCE exclusivity, thereby potentially facilitating generic competition. The FDA has also released a Drug Competition Action Plan, which proposes actions to broaden access to generic drugs and lower consumers' healthcare costs by, among other things, improving the efficiency of the generic drug approval process and supporting the development of complex generic drugs, and the FDA has taken and continues to take steps to implement this plan. Moreover, both Congress and the FDA are considering various legislative and regulatory proposals focused on drug competition, including legislation focused on drug patenting and provision of drug to generic applicants for testing. For example, the Further Consolidated Appropriations Act, 2020, which incorporated the framework from the Creating and Restoring Equal Access To Equivalent Samples (CREATES) legislation, was signed into law as part of the 2019 year-end federal spending package. The legislation purports to promote competition in the market for drugs and biological products by facilitating the timely entry of lower-cost generic and biosimilar versions of those drugs and biological products, including by allowing ANDA, 505(b)(2) NDA or biosimilar developers to obtain access to branded drug and biological product samples. While the full impact of these provisions is unclear at this time, its provisions do have the potential to facilitate the development and future approval of generic versions of our products, introducing generic competition that could have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Healthcare Regulatory and Other Legal Compliance Matters

We are subject to healthcare laws, regulations and enforcement; our failure to comply with those laws could have a material adverse impact on our business, financial condition and results of operations.

We are subject to federal and state healthcare laws and regulations, which laws and regulations are enforced by the federal government and the states in which we conduct our business. Should our compliance controls prove ineffective at preventing or mitigating the risk and impact of improper business conduct or inaccurate reporting, we could be subject to enforcement of the following, including, without limitation:

- the federal AKS;
- the FDCA and its implementing regulations;
- federal civil and criminal false claims laws, including the civil False Claims Act, and the Civil Monetary Penalties Law;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations, as amended;
- state law equivalents of each of the above federal laws;
- the Open Payments program of the PPACA;
- state and local laws and regulations that require drug manufacturers to file reports relating to marketing activities, payments and other remuneration and items of value provided to healthcare professionals and entities; and
- state and federal pharmaceutical price and price reporting laws and regulations.

In addition, we may be subject to the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, medical professionals employed by national healthcare programs) and its foreign equivalents, as well as federal and state consumer protection and unfair competition laws.

These federal and state healthcare laws and regulations govern drug marketing practices, including off-label promotion. If our operations are found, or even alleged, to be in violation of the laws described above or other governmental regulations that apply to us, we, or our officers or employees, may be subject to significant penalties, including administrative civil and criminal penalties, damages, fines, regulatory penalties, the curtailment or restructuring of our operations, exclusion from participation in Medicare, Medicaid and other federal and state healthcare programs, imprisonment, reputational harm, additional reporting requirements and oversight, any of which would adversely affect our ability to sell our products and operate our business and also adversely affect our financial results. Furthermore, responding to any such allegation and/or defending against any such enforcement actions can be time-consuming and would require significant financial and personnel resources. Therefore, if any state or the federal government initiates an enforcement action against us, our business may be impaired, and even if we are ultimately successful in our defense, litigating these actions could result in substantial costs and divert the attention of management.

Enhanced governmental and private scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer patient assistance programs and donations to patient assistance foundations created by charitable organizations could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

To help patients afford our products, we have a patient assistance program and also occasionally make donations to independent charitable foundations that help financially needy patients. These types of programs designed to assist patients with affording pharmaceuticals have become the subject of Congressional interest and enhanced government scrutiny. The HHS Office of Inspector General established guidelines permitting pharmaceutical manufacturers to make donations to charitable organizations that provide co-pay assistance to Medicare patients, provided that manufacturers meet certain specified compliance requirements. In the event we make such donations but are found not to have complied with these guidelines and other laws or regulations respecting the operation of these programs, we could be subject to significant damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We also rely on a third-party hub provider and exercise oversight to monitor patient assistance program activities. Hub providers are generally hired by manufacturers to assist patients with insurance coverage, financial assistance and treatment support after the patients receive a prescription from their healthcare professional. For manufacturers of specialty pharmaceuticals (including our marketed products), the ability to have a single point of contact for their therapies helps ensure efficient medication distribution to patients. Accordingly, our hub activities are also subject to scrutiny and may create risk for us if not conducted appropriately. A variety of entities, including independent charitable foundations and pharmaceutical manufacturers, but not including our company, have received subpoenas from the U.S. Department of Justice and other enforcement authorities seeking information related to their patient assistance programs and support. Should we or our hub providers receive a subpoena or other process, regardless of whether we are ultimately found to have complied with the regulations governing patient assistance programs, this type of government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

We are subject to laws and regulations relating to privacy, data protection and the collection and processing of personal data. Failure to maintain compliance with these regulations could create additional liabilities for us.

The legislative and regulatory landscape for privacy and data protection continues to evolve in the U.S. and other jurisdictions around the world. For example, the California Consumer Privacy Act of 2018 (CCPA) went into operation in 2020 and affords California residents expanded privacy rights and protections, including civil penalties for violations and statutory damages under a private right of action for data security breaches. These protections will be expanded by California Privacy Rights Act of 2020 (CPRA), which will be operational in most key respects on January 1, 2023. Similar legislative proposals have passed or are being advanced in other states, and Congress is also considering federal privacy legislation. In addition, most healthcare professionals and facilities are subject to privacy and security requirements under HIPAA. Although we are not considered to be a covered entity or business associate under HIPAA, we could be subject to penalties if we use or disclose individually identifiable health information in a manner not authorized or permitted by HIPAA. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. For example, the EU General Data Protection Regulation 2016/679 (GDPR) regulates the processing of personal data of individuals within the EU, even if, under certain circumstances, that processing occurs outside the EU, and also places restrictions on transfers of such data to countries outside of the EU, including the U.S. Should we fail to provide adequate privacy or data security protections or maintain compliance with these laws and regulations, including the CCPA, CPRA and GDPR, we could be subject to sanctions or other penalties, litigation or an increase in our cost of doing business.

Risks Related to Growth of Our Product Portfolio and Research and Development

Clinical testing of cabozantinib for new indications, or of new product candidates, is a lengthy, costly, complex and uncertain process that may fail ultimately to demonstrate safety and efficacy data for those products sufficiently differentiated to compete in our highly competitive market environment.

Clinical trials are inherently risky and may reveal that cabozantinib, despite its approval for certain indications, or a new product candidate, is ineffective or has an unacceptable safety profile with respect to an intended use. Such results may significantly decrease the likelihood of regulatory approval of a product candidate or of an approved product for a new indication. Moreover, the results of preliminary studies do not necessarily predict clinical or commercial success, and late-stage or other potentially label-enabling clinical trials may fail to confirm the results observed in early-stage trials or preliminary studies. Although we have established timelines for manufacturing and clinical development of cabozantinib and our other product candidates based on existing knowledge of our compounds in development and industry metrics, we may not be able to meet those timelines.

We may experience numerous unforeseen events, during or as a result of clinical investigations, that could delay or prevent commercialization of cabozantinib in new indications or of new product candidates, and in some cases, as described in the risk factor titled, "*If the COVID-19 pandemic is further prolonged or becomes more severe, our business operations and corresponding financial results could suffer, which could have a material adverse impact on our financial condition and prospects for growth,*" the COVID-19 pandemic has already increased and may further increase the potential for such events to occur. These events may include:

- lack of acceptable efficacy or a tolerable safety profile;
- negative or inconclusive clinical trial results that require us to conduct further testing or to abandon projects;
- discovery or commercialization by our competitors of other compounds or therapies that show significantly improved safety or efficacy compared to cabozantinib or our other product candidates;
- our inability to identify and maintain a sufficient number of trial sites;
- lower-than-anticipated patient registration or enrollment in our clinical testing;
- additional complexities posed by clinical trials evaluating cabozantinib or our other product candidates in combination with other therapies, including extended timelines to provide for collaboration on clinical development planning, the failure by our collaboration partners to provide us with an adequate and timely supply of product that complies with the applicable quality and regulatory requirements for a combination trial;
- failure of our third-party contract research organizations or investigators to satisfy their contractual obligations, including deviating from any trial protocols; and
- withholding of authorization from regulators or institutional review boards to commence or conduct clinical trials or delays, suspensions or terminations of clinical research for various reasons, including noncompliance with regulatory requirements or a determination by these regulators and institutional review boards that participating patients are being exposed to unacceptable health risks.

If there are further delays in or termination of the clinical testing of cabozantinib or our other product candidates due to any of the events described above or otherwise, our expenses could increase and our ability to generate revenues could be impaired, either of which could adversely impact our financial results. Furthermore, we rely on our collaboration partners to fund a significant portion of our clinical development programs. Should one or all of our collaboration partners decline to support future planned clinical trials, we will be entirely responsible for financing the further development of the cabozantinib franchise or our other product candidates and, as a result, we may be unable to execute our current business plans, which could have a material adverse impact on our business, financial condition and results of operations.

We may not be able to pursue the further development of the cabozantinib franchise or our other product candidates or meet current or future requirements of the FDA or regulatory authorities in other jurisdictions in accordance with our stated timelines or at all. Our planned clinical trials may not begin on time, or at all, may not be completed on schedule, or at all, may not be sufficient for registration of our product candidates or may not result in an approvable product. The duration and the cost of clinical trials vary significantly as a result of factors relating to the clinical trial, including, among others: the characteristics of the product candidate under investigation; the number of patients who ultimately participate in the clinical trial; the duration of patient follow-up; the number of clinical sites included in the trials; and the length of time required to enroll eligible patients.

Any delay could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly. Our partners under our collaboration agreements may experience similar risks with respect to the compounds we have out-licensed to them. If any of the events described above were to occur with such programs or compounds, the likelihood of receipt of milestones and royalties under such collaboration agreements could decrease.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy and uncertain and may not result in regulatory approvals for additional cabozantinib indications or our other product candidates, which could have a material adverse impact on our business, financial condition and results of operations.

The activities associated with the research, development and commercialization of the cabozantinib franchise and our other product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the U.S., as well as by comparable regulatory authorities in other territories. The processes of obtaining regulatory approvals in the U.S. and other foreign jurisdictions is expensive and often takes many years, if approval is obtained at all, and they can vary substantially based upon the type, complexity and novelty of the product candidates involved. For example, before an NDA or sNDA can be submitted to the FDA, or a marketing authorization application to the EMA or any application or submission to comparable regulatory authorities in other jurisdictions, the product candidate must undergo extensive clinical trials, which can take many years and require substantial expenditures.

Any clinical trial may fail to produce results satisfactory to the FDA or regulatory authorities in other jurisdictions. The FDA has substantial discretion in the approval process and may refuse to approve any NDA or sNDA or decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, we may encounter delays or rejections based upon changes in policy, which could cause delays in the approval or rejection of an application for cabozantinib or for our other product candidates.

Even if the FDA or a comparable authority in another jurisdiction approves cabozantinib for one or more new indications, such approval may be limited, imposing significant restrictions on the indicated uses, conditions for use, labeling, distribution, and/or production of the product and could impose requirements for post-marketing studies, including additional research and clinical trials, all of which may result in significant expense and limit our and our collaboration partners' ability to commercialize cabozantinib in one or more new indications. Failure to complete post-marketing requirements of the FDA in connection with a specific approval in accordance with the timelines and conditions set forth by the FDA could significantly increase costs or delay, limit or ultimately restrict the commercialization of cabozantinib in that indication. Regulatory agencies could also impose various administrative, civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval. Further, current or any future laws or executive orders governing FDA or foreign regulatory approval processes that may be enacted or executed, including in response to the COVID-19 pandemic could have a material adverse impact on our business, financial condition, and results of operations.

We may be unable to expand our development pipeline, which could limit our growth and revenue potential.

Our business is focused on the discovery, development and commercialization of new medicines for difficult-to-treat cancers. In this regard, we have invested in substantial technical, financial and human resources toward drug discovery activities with the goal of identifying new product candidates to advance into clinical trials. Notwithstanding this investment, many programs that initially show promise will ultimately fail to yield product candidates for multiple reasons. For example, product candidates may, on further study, be shown to have inadequate efficacy, harmful side effects, suboptimal pharmaceutical profiles or other characteristics suggesting that they are unlikely to be commercially viable products.

Apart from our drug discovery efforts, our strategy to expand our development pipeline is also dependent on our ability to successfully identify and acquire or in-license relevant product candidates and technologies. However, the in-licensing and acquisition of product candidates and technologies is a highly competitive area, and many other companies are pursuing the same or similar product candidates and technologies to those that we may consider attractive. In particular, larger companies with more capital resources and more extensive clinical development and commercialization capabilities may have a competitive advantage over us. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to in-license or acquire additional product candidates and technologies on acceptable terms that would allow us to realize an appropriate return on our investment. Even if we succeed in our efforts to obtain rights to suitable product candidates and technologies, the competitive business environment may result in higher acquisition or licensing costs, and our investment in these potential products and technologies will remain subject to the inherent risks associated with the development and commercialization of new medicines. In certain circumstances, we may also be reliant on the licensor for the continued development of the in-licensed technology and their efforts to safeguard their underlying intellectual property.

With respect to acquisitions, we may not be able to integrate the target company successfully into our existing business, maintain the key business relationships of the target company, or retain key personnel of the acquired business. Furthermore, we could assume unknown or contingent liabilities or otherwise incur unanticipated expenses. Any acquisitions or investments made by us also could result in our spending significant amounts, issuing dilutive securities, assuming or incurring significant debt obligations and contingent liabilities, incurring large one-time expenses and acquiring intangible assets that could result in significant future amortization expense and significant write-offs, any of which could harm our financial condition and results of operations. If our drug discovery efforts, including research collaborations, in-licensing arrangements and other business development activities, do not result in suitable product candidates, our business and prospects for growth could suffer.

Risks Related to Financial Matters and Capital Requirements

Our profitability could be negatively impacted if expenses associated with our extensive clinical development, business development and commercialization activities, both for the cabozantinib franchise and our earlier-stage product candidates, grow more quickly than the revenues we generate.

Although we reported net income of $38.2 million and $135.9 million for the three and nine months ended September 30, 2021 and $111.8 million for the year ended December 31, 2020, we may not be able to maintain or increase profitability on a quarterly or annual basis, and we are unable to predict the extent of future profits or losses. The amount of our net profits or losses will depend, in part, on: the level of sales of CABOMETYX and COMETRIQ in the U.S.; our achievement of clinical, regulatory and commercial milestones, if any, under our collaboration agreements; the amount of royalties from sales of CABOMETYX and COMETRIQ outside of the U.S. under our collaboration agreements; other collaboration revenues; and the level of our expenses, including those associated with our extensive drug discovery, clinical development, business development and commercialization activities, both for the cabozantinib franchise and our earlier-stage product candidates. For example, we reported a net loss for the quarter ended September 30, 2020, primarily due to substantial increases in clinical trial costs, license and other collaboration costs, and personnel expenses relative to the prior fiscal quarters, and it is possible that we may experience net losses in future fiscal quarters or fiscal years, whether due to increases in costs and expenses or otherwise. We expect to continue to spend substantial amounts to fund the continued development of the cabozantinib franchise for additional indications and the commercialization of our approved products. In addition, we intend to continue to expand our oncology product pipeline through our drug discovery efforts, including research collaborations, in-licensing arrangements and other business development activities that align with our oncology drug development, regulatory and commercial expertise, which efforts could involve substantial costs. To offset these costs in the future, we will need to generate substantial revenues. If these costs exceed our current expectations, or we fail to achieve anticipated revenue targets, the market value of our common stock may decline.

If additional capital is not available to us when we need it, we may be unable to expand our product offerings and maintain business growth.

Our commitment of cash resources to CABOMETYX and the reinvestment in our product pipeline through the continued development of the cabozantinib franchise and increasing drug discovery activities, as well as through the execution of business development transactions, could require us to obtain additional capital. We may seek such additional capital through some or all of the following methods: corporate collaborations; licensing arrangements; and public or private debt or equity financings. Our ability to obtain additional capital may depend on prevailing economic conditions and financial, business and other factors beyond our control. Disruptions in the U.S. and global financial markets, including disruptions that have resulted and may continue to result from the COVID-19 pandemic and the related volatility in the U.S. and global economy, as well as future potential U.S. federal government shutdowns, rising interest rate environments, inflation rates, increased or changed tariffs and trade restrictions or otherwise, may adversely impact the availability and cost of credit, as well as our ability to raise additional funds in the capital markets. Economic and capital markets conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to access the capital necessary to fund and grow our business. In particular, our inability to access additional funds, whether due to the COVID-19 pandemic or otherwise, could in the future inhibit our ability to engage in larger-scale strategic transactions or investments. We do not know whether additional capital will be available when needed, or that, if available, we will obtain additional capital on terms favorable to us or our stockholders. If we are unable to raise additional funds when we need them, we may be unable to expand our product offerings and maintain business growth, which could have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Our Relationships with Third Parties

We rely on Ipsen and Takeda for the commercial success of CABOMETYX in its approved indications outside of the U.S., and we are unable to control the amount or timing of resources expended by these collaboration partners in the commercialization of CABOMETYX in its approved indications outside of the U.S.

We rely upon the regulatory, commercial, medical affairs, market access and other expertise and resources of our collaboration partners, Ipsen and Takeda, for commercialization of CABOMETYX in their respective territories outside of the U.S. We cannot control the amount and timing of resources that our collaboration partners dedicate to the commercialization of CABOMETYX, or to its marketing and distribution, and our ability to generate revenues from the commercialization of CABOMETYX by our collaboration partners depends on their ability to obtain and maintain regulatory approvals for, achieve market acceptance of, and to otherwise effectively market, CABOMETYX in its approved indications in their respective territories. Further, the operations of our collaboration partners, and ultimately their sales of CABOMETYX in their respective territories outside of the U.S., could be adversely affected by the degree and effectiveness of their respective corporate responses to the COVID-19 pandemic, as well as by the imposition of governmental price or other controls, political and economic instability, trade restrictions or barriers and changes in tariffs, escalating global trade and political tensions, or other factors. If our collaboration partners are unable or unwilling to invest the resources necessary to commercialize CABOMETYX successfully in the EU, Japan and other international territories where it has been approved, this could reduce the amount of revenue we are due to receive under these collaboration agreements, thus resulting in harm to our business and operations.

Our clinical, regulatory and commercial collaborations with major companies make us reliant on those companies for their continued performance and investments, which subjects us to a number of risks.

We have established clinical and commercial collaborations with leading biotechnology, biopharmaceutical and pharmaceutical companies for the development and commercialization of our products, and our dependence on these collaboration partners subjects us to a number of risks, including, but not limited to:

- our collaboration partners' decision to terminate our collaboration, or their failure to comply with the terms of our collaboration agreements and related ancillary agreements, either intentionally or as a result of negligent performance;
- our inability to control the amount and timing of resources that our collaboration partners devote to the development or commercialization of our products;
- the possibility that our collaboration partners may stop or delay clinical trials, fail to supply us on a timely basis with product required for a combination trial (including as a result of the COVID-19 pandemic), or deliver product that fails to meet appropriate quality and regulatory standards;
- disputes that may arise between us and our collaboration partners that result in the delay or termination of the development or commercialization of our drug candidates, or that diminish or delay receipt of the economic benefits we are entitled to receive under the collaboration, or that result in costly litigation or arbitration;
- the possibility that our collaboration partners may experience financial difficulties, including, without limitation, difficulties arising from the impact of the COVID-19 pandemic that prevent them from fulfilling their obligations under our agreements;
- our collaboration partners' inability to obtain regulatory approvals in a timely manner, or at all;
- our collaboration partners' failure to comply with legal and regulatory requirements relevant to the authorization, marketing, distribution and supply of our marketed products in the territories outside the U.S. where they are approved; and
- our collaboration partners' failure to properly maintain or defend our intellectual property rights or their use of our intellectual property rights or proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential litigation.

If any of these risks materialize, we may not receive collaboration revenues or otherwise realize anticipated benefits from such collaborations, and our product development efforts and prospects for growth could be delayed or disrupted, all of which could have a material adverse impact on our business, financial condition and results of operations.

Our growth potential is dependent in part upon companies with which we have entered into research collaborations, in-licensing arrangements and similar business development relationships.

To expand our early-stage product pipeline, we have augmented our drug discovery activities with multiple research collaborations and in-licensing arrangements with other companies. Our dependence on our relationships with these research and in-licensing partners subjects us to numerous risks, including, but not limited to:

- our research and in-licensing partners' decision to terminate our relationship, or their failure to comply with the terms of our agreements, either intentionally or as a result of negligent performance;
- disputes that may arise between us and our research and in-licensing partners that result in the delay or termination of research activities with respect to any in-licensed assets or supporting technology platforms;

- the possibility that our research and in-licensing partners may experience financial difficulties, including, without limitation, difficulties arising from the impact of the COVID-19 pandemic, which prevent them from fulfilling their obligations under our agreements;
- our research and in-licensing partners' failure to properly maintain or defend their intellectual property rights or their use of third-party intellectual property rights or proprietary information in such a way as to invite litigation that could jeopardize or invalidate our license to develop these assets or utilize technology platforms;
- laws, regulations or practices imposed by countries outside the U.S. that could impact or inhibit scientific research or the development of healthcare products by foreign competitors or otherwise disadvantage healthcare products made by foreign competitors, as well as general political or economic instability in those countries, any of which could complicate, interfere with or impede our relationships with our ex-U.S. research, development and in-licensing partners; and
- our research and in-licensing partners' failure to comply with applicable healthcare laws, as well as established guidelines, laws and regulations related to Good Manufacturing Practice and Good Laboratory Practice.

If any of these risks materialize, we may not be able to expand our product pipeline or otherwise realize a return on the resources we will have invested to develop these early-stage assets, which could have a material adverse impact on our financial condition and prospects for growth.

If third parties upon which we rely to perform clinical trials for cabozantinib in new indications or for new product candidates do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize cabozantinib or other product candidates beyond currently approved indications.

We do not have the ability to conduct clinical trials for cabozantinib or for new potential product candidates independently, so we rely on independent third parties for the performance of these trials, such as the U.S. federal government (including NCI-CTEP, a department of the National Institutes of Health, with whom we have our CRADA), third-party contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, whether as a result of the COVID-19 pandemic or otherwise, or if the third parties must be replaced or if the quality or accuracy of the data they generate or provide is compromised due to their failure to adhere to our clinical trial or data security protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or commercialize cabozantinib beyond currently approved indications or obtain regulatory approval for our other product candidates. In addition, due to the complexity of our research initiatives, we may be unable to engage with third-party contract research organizations that have the necessary experience and sophistication to help advance our drug discovery efforts, which would impede our ability to identify, develop and commercialize our potential product candidates.

We lack our own manufacturing and distribution capabilities necessary for us to produce materials required for certain preclinical activities and to produce and distribute our products for clinical development or for commercial sale, and our reliance on third parties for these services subjects us to various risks.

We do not own or operate manufacturing facilities, distribution facilities or resources for chemistry, manufacturing and control development activities, preclinical, clinical or commercial production and distribution for our current products and new product candidates. Instead, we rely on various third-party contract manufacturing organizations to conduct these operations on our behalf. As our operations continue to grow in these areas, we continue to expand our supply chain through secondary third-party contract manufacturers, distributors and suppliers. To establish and manage our supply chain requires a significant financial commitment, the creation of numerous third-party contractual relationships and continued oversight of these third parties to fulfill compliance with applicable regulatory requirements. Although we maintain significant resources to directly and effectively oversee the activities and relationships with the companies in our supply chain, we do not have direct control over their operations.

Our third-party contract manufacturers may not be able to produce material on a timely basis or manufacture material with the required quality standards, or in the quantity required to meet our preclinical, clinical development and commercial needs and applicable regulatory requirements, including as a result of the COVID-19 pandemic. Although we have not yet experienced production delays or seen significant impairment to our supply chain as a result of the COVID-19 pandemic, our third-party contract manufacturers, distributors and suppliers could experience operational delays due to facility closures and other hardships as a result of the COVID-19 pandemic, which could impact our supply chain by potentially causing delays to or disruptions in the supply of our commercial or clinical products or product candidates. If our third-party contract manufacturers, distributors and suppliers do not continue to supply us with our products or product candidates in a timely fashion and in compliance with applicable quality and regulatory requirements, or if they otherwise fail or refuse to comply with their obligations to us under our manufacturing, distribution and supply arrangements, we may not have adequate remedies for any breach. Furthermore, their failure to supply us could impair or preclude meeting commercial or clinical product supply requirements for us or our partners, which could delay product development and future commercialization efforts and have a material adverse impact on our business, financial condition and results of operations. In addition, through our third-party contract manufacturers and data service providers, we continue to provide serialized commercial products as required to comply with the Drug Supply Chain Security Act (DSCSA). If our third-party contract manufacturers or data service providers fail to support our efforts to continue to comply with DSCSA and any future federal or state electronic pedigree requirements, we may face legal penalties or be restricted from selling our products.

If third-party scientific advisors and contractors we rely on to assist with our drug discovery efforts do not perform as expected, the expansion of our product pipeline may be delayed.

We work with scientific advisors at academic and other institutions, as well as third-party contractors in various locations throughout the world, that assist us in our research and development efforts, including in drug discovery and preclinical development strategy. These third parties are not our employees and may have other commitments or contractual obligations that limit their availability to us. Although these third-party scientific advisors and contractors generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. There has also been increased scrutiny surrounding the disclosures of payments made to medical researchers from companies in the pharmaceutical industry, and it is possible that the academic and other institutions that employ these medical researchers may prevent us from engaging them as scientific advisors and contractors or otherwise limit our access to these experts, or that the scientific advisors themselves may now be more reluctant to work with industry partners. Even if these scientific advisors and contractors with whom we have engaged intend to meet their contractual obligations, their ability to perform services may be impacted by increased demand for such services from other companies or by other external factors, such as reduced capacity to perform services, as we experienced in the early stages of the COVID-19 pandemic. If we experience additional delays in the receipt of services, lose work performed by these scientific advisors and contractors or are unable to engage them in the first place, our discovery and development efforts with respect to the matters on which they were working or would work in the future may be significantly delayed or otherwise adversely affected.

Risks Related to Our Information Technology and Intellectual Property

Data breaches, cyber-attacks and other failures in our information technology operations and infrastructure could compromise our intellectual property or other sensitive information, damage our operations and cause significant harm to our business and reputation.

In the ordinary course of our business, we and our third-party service providers, such as contract research organizations, collect, maintain and transmit sensitive data on our networks and systems, including our intellectual property and proprietary or confidential business information (such as research data and personal information) and confidential information with respect to our customers, clinical trial patients and our collaboration partners. We have also outsourced significant elements of our information technology infrastructure to third parties and, as a result, such third parties may or could have access to our confidential information. The secure maintenance of this information is critical to our business and reputation, and while we have enhanced and are continuing to enhance our cybersecurity efforts commensurate with the growth and complexity of our business, our systems and those of third-party service providers may be vulnerable to a cyber-attack. The level of vulnerabilities that exist under normal conditions may have been exacerbated by the fact that, during the COVID-19 pandemic, the portion of our workforce operating remotely has increased, at least temporarily, and some phishing attacks are specifically designed to target remote workers. In addition, we are heavily dependent on the functioning of our information technology infrastructure to carry out our business processes, such as external and internal communications or access to clinical data and other key business information. Accordingly, both inadvertent disruptions to this infrastructure and cyber-attacks could cause us to incur significant remediation or litigation costs, result in product development delays, disrupt critical business operations, expend key information technology resources and divert the attention of management.

Although the aggregate impact of cyber-attacks on our operations and financial condition has not been material to date, we and our third-party service providers have frequently been the target of threats of this nature and expect them to continue. Any data breach and/or unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose our sensitive business information or sensitive business information of our collaboration partners, which may lead to significant liability for us. A data security breach could also lead to public exposure of personal information of our clinical trial patients, employees or others and result in harm to our reputation and business, compel us to comply with federal and/or state breach notification laws and foreign law equivalents including the GDPR, subject us to investigations and mandatory corrective action, or otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could disrupt our business, result in increased costs or loss of revenue, and/or result in significant financial exposure. Furthermore, the costs of maintaining or upgrading our cybersecurity systems (including the recruitment and retention of experienced information technology professionals, who are in high demand) at the level necessary to keep up with our expanding operations and prevent against potential attacks are increasing, and despite our best efforts, our network security and data recovery measures and those of our third-party service providers may still not be adequate to protect against such security breaches and disruptions, which could cause material harm to our business, financial condition and results of operations.

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could adversely affect our ability to compete in the market.

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biopharmaceutical companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as, where and when we deem lawful and appropriate. However, these applications may be challenged or may fail to result in issued patents. Our issued patents have been and may in the future be challenged by third parties as invalid or unenforceable under U.S. or foreign laws, or they may be infringed by third parties, and we are from time to time involved in the defense and enforcement of our patents or other intellectual property rights in a court of law, U.S. Patent and Trademark Office *inter partes* review or reexamination proceeding, foreign opposition proceeding or related legal and administrative proceeding in the U.S. and elsewhere. The costs of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings and litigation can be substantial and the outcome can be uncertain. An adverse outcome may allow third parties to use our intellectual property without a license and/or allow third parties to introduce generic and other competing products, any of which would negatively impact our business. Third parties may also attempt to invalidate or design around our patents, or assert that they are invalid or otherwise unenforceable, and seek to introduce generic versions of cabozantinib. For example, we received Paragraph IV certification notice letters from MSN and Teva concerning the respective ANDAs that each had filed with the FDA seeking approval to market their respective generic versions of CABOMETYX tablets. Should MSN, Teva or any other third parties receive FDA approval of an ANDA or a 505(b)(2) NDA with respect to cabozantinib, it is possible that such company or companies could introduce generic versions of our marketed products before our patents expire if they do not infringe our patents or if it is determined that our patents are invalid or unenforceable, and the resulting generic competition could have a material adverse impact on our business, financial condition and results of operations.

In addition, because patent applications can take many years to issue, third parties may have pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. They may also be negatively impacted by the decisions of foreign courts, which could limit the protection contemplated by the original regulatory approval and our ability to thwart the development of competing products that might otherwise have been determined to infringe our intellectual property rights. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for closely related inventions.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S., and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to “work” the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Initiatives seeking compulsory licensing of life-saving drugs are also becoming increasingly prevalent in developing countries either through direct legislation or international initiatives. Governments in those developing countries could require that we grant compulsory licenses to allow competitors to manufacture and sell their own versions of our products or product candidates, thereby reducing our product sales. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. We also rely on trade secret protection for some of our confidential and proprietary information, and we have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees, partners and consultants, we cannot provide assurance that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

Litigation or third-party claims of intellectual property infringement could require us to spend substantial time and money and adversely affect our ability to develop and commercialize products.

Our commercial success depends in part upon our ability to avoid infringing patents and proprietary rights of third parties and not to breach any licenses that we have entered into with regard to our technologies and the technologies of third parties. Other parties have filed, and in the future are likely to file, patent applications covering products and technologies that we have developed or intend to develop. If patents covering technologies required by our operations are issued to others, we may have to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, and may require us to pay substantial royalties, grant a cross-license to some of our patents to another patent holder or redesign the formulation of a product candidate so that we do not infringe third-party patents, which may be impossible to accomplish or could require substantial time and expense. In addition, we may be subject to claims that our employees or independent contractors have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that they used or sought to use patent inventions belonging to their former employers. Furthermore, third parties may obtain patents that relate to our technologies and claim that use of such technologies infringes on their patents or otherwise employs their proprietary technology without authorization. Regardless of their merit, such claims could require us to incur substantial costs and divert the attention of management and key technical personnel in defending ourselves against any such claims or enforcing our own patents. In the event of any third party's successful claim of patent infringement or misappropriation of trade secrets, we may lose valuable intellectual property rights or personnel, which could impede or prevent the achievement of our product development goals, or we may be required to pay damages and obtain one or more licenses from these third parties, subjecting us to substantial royalty payment obligations. We may not be able to obtain these licenses on commercially reasonable terms, or at all. Defense of any lawsuit or failure to obtain any of these licenses could adversely affect our ability to develop and commercialize products.

Risks Related to Our Operations, Managing Our Growth and Employee Matters

If the COVID-19 pandemic is further prolonged or becomes more severe, our business operations and corresponding financial results could suffer, which could have a material adverse impact on our financial condition and prospects for growth.

To date, the COVID-19 pandemic has had a modest impact on our business operations, in particular with respect to our clinical trial, drug discovery and commercial activities. For example, to varying degrees and at different rates across our clinical trials, we experienced declines in screening and enrollment activity during the early days of the COVID-19 pandemic, as well as delays in new site activations and restrictions on the access to treatment sites that is necessary to monitor clinical study progress and administration. As the COVID-19 pandemic continues to have a significant presence in various parts of the world, particularly with the emergence of the Delta variant and other SARS-CoV-2 variants, the impact on our clinical development operations could continue or grow more severe. We anticipate that a further prolonged, or more severe, global public health crisis could limit our ability to identify and work with clinical investigators at clinical trial sites globally to enroll, initiate and maintain treatment per protocol of patients for our ongoing clinical trials. Disruptions to medical and administrative operations at clinical trial sites and the implementation of crisis management initiatives have and may continue to reduce personnel and other resources necessary to conduct our clinical trials, which could delay our clinical trial plans or require certain trials to be temporarily suspended. Moreover, quarantines and travel restrictions have impeded and may continue to impede patient movement or interrupt healthcare services, which we anticipate over time, could also interfere with and potentially negatively impact clinical trial execution, and ultimately results. In addition, increased costs connected with our efforts to mitigate the adverse impacts resulting from the COVID-19 pandemic on our clinical trials could cause the expenses we incur in conducting those clinical trials to increase considerably. Specifically, with respect to our clinical trials evaluating cabozantinib in combination with therapies that must be administered via professional intravenous infusion, such as COSMIC-313, COSMIC-021, CONTACT-01, CONTACT-02, CONTACT-03, our early-stage trials evaluating XL092, XL102 and other product candidates to the extent they may incorporate additional therapies that must be administered via professional intravenous infusion, or our early-stage trial evaluating XB002 that must be administered via professional intravenous infusion, limited patient movement or interrupted healthcare services at medical institutions have delayed in some instances, and may continue to delay or prevent, on-site infusion of XB002 or therapies being evaluated in combination with cabozantinib or our other product candidates. If a sizable portion of patients in our combination studies are unable or unwilling to receive all components of the combination therapy being tested in accordance with the applicable clinical trial protocol, it could cause those studies to be delayed, suspended or prevented from producing statistically significant results. Depending upon the duration and severity of the COVID-19 pandemic, we could also experience delays in the commencement of new clinical trials of cabozantinib, or our earlier-stage investigative product candidates. The COVID-19 pandemic could also impede clinical operations and delay our planning and preparation timelines for new clinical trials, as well as adversely affect our ability to obtain regulatory approval for clinical protocols and increase the operating expenses associated with these new clinical trials.

In addition, the COVID-19 pandemic caused us to suspend drug discovery work in our laboratories temporarily while we observed the shelter in place orders issued by the State of California and Alameda County. We also experienced some modest delays with respect to the portion of drug discovery work outsourced to third-party contractors in regions first impacted by COVID-19. While both drug discovery work in our laboratories and outsourced drug discovery activities have since fully resumed, we may be unable to maximize the potential of these programs due to the imposition of increased safety protocols, and should the COVID-19 pandemic grow in severity, we may have to again scale back or suspend activities in the future. We are also reliant on laboratory materials manufactured and distributed from areas impacted by both the COVID-19 pandemic and other natural disasters, for which supply has become limited. If we are unable to obtain the requisite materials to conduct our planned drug discovery activities, we may be required to redirect the focus of, or even suspend, such activities. With respect to the preclinical development work and drug discovery activities outsourced to third-party contractors, the COVID-19 pandemic could again impede these third parties from providing timely deliverables to us in the future. Should the COVID-19 pandemic be further prolonged or grow in severity, we may ultimately be unable to achieve our drug discovery and preclinical development objectives within the previously disclosed timelines, which could have a material adverse impact on our prospects for growth.

While we believe that our commercial business has, to date, only experienced a modest impact related to the COVID-19 pandemic, it remains possible that over a longer period, changes to our standard sales and marketing practices, including any shifts from in-person back to primarily telephonic and virtual interactions with healthcare professionals, could negatively impact the flow of important information regarding our medicines, which along with obstacles to patient access to healthcare professionals, could diminish sales of our marketed products.

Although as of the date of this Quarterly Report on Form 10-Q, we continue to maintain sufficient safety stock inventories for our drug substance and drug products and have not experienced production delays or seen significant impairment to our supply chain as a result of the COVID-19 pandemic, our third-party contract manufacturers and suppliers could experience operational delays due to facility closures and other hardships as a result of the COVID-19 pandemic, which could impact our supply chain by potentially causing delays to or disruptions in the supply of our commercial or clinical products or product candidates. These delays or disruptions could be further exacerbated if the COVID-19 pandemic begins to impact essential distribution systems, which could substantially increase delivery times and costs, or otherwise adversely affect our ability to provide our products to customers and clinical trial sites and generate product revenues.

In response to the COVID-19 pandemic, we have taken numerous precautions, some temporary and others still in place, to help mitigate the risk of transmission of the virus in the workplace, including: initially reducing the number of our employees working on-site at our Alameda headquarters; implementing a vaccination mandate and maintaining enhanced safety and social distancing protocols for those employees who have returned to working on-site, as well as initiating an on-site COVID-19 testing program; limiting certain non-essential business travel for our employees; and partially limiting the circumstances under which our field employees may engage in in-person promotional activities with healthcare professionals. Over a longer period, these measures could delay our research and development programs, reduce engagements with potential prescribers for our products, and impede our ability to execute on our long-term business plans. Further, even though our Alameda-based workforce has largely returned to working on-site at our headquarters consistent with the policies in place prior to the COVID-19 pandemic, future periods of primarily remote work, if necessitated by the circumstances surrounding the COVID-19 pandemic, could impede the focused attention of management or reduce the productivity of teams that would otherwise be working closely together.

In addition, as a result of broad economic shifts during and as a consequence of efforts to address unemployment and other negative economic effects of the COVID-19 pandemic, we may experience reductions in the net price of our products. For example, there may be a substantial shift from private health insurance coverage to government insurance coverage, or additional downward pressure on the prices government purchasers will pay for our products due to significant increases in government debt incurred in connection with relief efforts, as well as significant increases in demand for our patient assistance and/or free drug program or other impacts that may not be foreseeable, all or any of which would adversely affect our product revenues.

While we expect the COVID-19 pandemic to continue to have varying degrees of adverse impact on our business operations and, potentially in the future, our financial results, the extent of such adverse impact will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time. Such developments include continued spread of the Delta variant in the U.S. and other countries and the potential emergence of other SARS-CoV-2 variants that may prove especially contagious or virulent, the ultimate duration of the pandemic and resulting disruptions to normal business and personal activities in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat the disease, including the rate at which vaccinations are made available and are administered, the percentage of the population that becomes fully vaccinated and the effectiveness of the vaccines against Delta or other SARS-CoV-2 variants. These continuing or future effects could materially and adversely affect our business, financial condition, results of operations and growth prospects, and exacerbate the other risks and uncertainties described elsewhere in this ‘‘Risk Factors’’ section.

If we are unable to manage our growth, there could be a material adverse impact on our business, financial condition and results of operations, and our prospects may be adversely affected.

We have experienced and expect to continue to experience growth in the number of our employees and in the scope of our operations, in particular as we continue to expand the cabozantinib franchise into new indications and grow our pipeline of product candidates. This growth places significant demands on our management and resources, and our current and planned personnel and operating practices may not be adequate to support our growth. To effectively manage our growth, we must continue to improve existing, and implement new, facilities, operational and financial systems, and procedures and controls, as well as expand, train and manage our growing employee base, and there can be no assurance that we will effectively manage our growth without experiencing operating inefficiencies or control deficiencies. We continue to increase our management personnel to oversee our expanding operations, and recruiting and retaining qualified individuals is difficult. If we are unable to manage our growth effectively, including as a result of the COVID-19 pandemic or otherwise, or we are unsuccessful in recruiting qualified management personnel, there could be a material adverse impact on our business, financial condition and results of operations.

The loss of key personnel or the inability to retain and, where necessary, attract additional personnel could impair our ability to operate and expand our operations.

We are highly dependent upon the principal members of our management, as well as clinical, commercial and scientific staff, the loss of whose services might adversely impact the achievement of our objectives. For example, in September 2021, we announced the passing of Dr. Gisela Schwab, our President, Product Development and Medical Affairs and Chief Medical Officer, and Jon Berndt, our Senior Vice President, Sales. While we have continued to execute on our clinical development and commercial strategies, have filled the sales leadership position and are conducting a search to fill the Chief Medical Officer position, we cannot ensure that the losses of Dr. Schwab and Mr. Berndt will not negatively impact our business and operations. Also, we may not have sufficient personnel to execute our business plans. Retaining and, where necessary, recruiting qualified clinical, commercial, scientific and pharmaceutical operations personnel will be critical to support activities related to advancing the development program for the cabozantinib franchise and our other product candidates, successfully executing upon our commercialization plan for the cabozantinib franchise and our proprietary research and development efforts. Competition is intense for experienced clinical, commercial, scientific and pharmaceutical operations personnel, and we may be unable to retain or recruit such personnel with the expertise or experience necessary to allow us to successfully develop and commercialize our products. Similarly, the COVID-19 pandemic could negatively impact the health of key personnel or make it difficult to recruit qualified personnel for critical positions. Further, all of our employees are employed “at will” and, therefore, may leave our employment at any time.

Risks Related to Environmental and Product Liability

We use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and biological materials, and our operations can produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge, or any resultant injury from these materials, and we may face liability under applicable laws for any injury or contamination that results from our use or the use by our collaboration partners or other third parties of these materials. Such liability may exceed our insurance coverage and our total assets, and in addition, we may be required to indemnify our collaboration partners against all damages and other liabilities arising out of our development activities or products produced in connection with our collaborations with them. Moreover, our continued compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

We face potential product liability exposure far in excess of our limited insurance coverage.

We may be held liable if any product we or our collaboration partners develop or commercialize causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our products and product candidates, injury to our reputation, withdrawal of patients from our clinical trials, product recall, substantial monetary awards to third parties and the inability to commercialize any products that we may develop in the future. We maintain limited product liability insurance coverage for our clinical trials and commercial activities for cabozantinib. However, our insurance may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability.

Risks Related to Our Common Stock

Our stock price has been and may in the future be highly volatile.

The trading price of our common stock has been highly volatile, and it may remain highly volatile or fluctuate substantially due to factors such as the following, many of which we cannot control:

- the announcement of FDA or other regulatory approval or non-approval, or delays in the FDA or other regulatory review process with respect to cabozantinib, our collaboration partners’ product candidates being developed in combination with cabozantinib, or our competitors’ product candidates;
- the commercial performance of both CABOMETYX and COMETRIQ and the revenues we generate from those approved products, including royalties paid under our collaboration and license agreements;
- adverse or inconclusive results or announcements related to our or our collaboration partners’ clinical trials or delays in those clinical trials;
- the timing of achievement of our clinical, regulatory, partnering, commercial and other milestones for the cabozantinib franchise or any of our other programs or product candidates;
- our ability to make future investments in the expansion of our pipeline through drug discovery, including future research collaborations, in-licensing arrangements and other business development activities;
- our ability to obtain the materials and services, including an adequate product supply for any approved drug product, from our third-party vendors or do so at acceptable prices;
- the timing and amount of expenses incurred for clinical development and manufacturing of cabozantinib;
- actions taken by regulatory agencies, both in the U.S. and abroad, with respect to cabozantinib or our clinical trials for cabozantinib;
- unanticipated regulatory actions taken by the FDA as a result of changing FDA standards and practices concerning the review of product candidates, including approvals at earlier stages of clinical development or with lesser developed data sets and expedited reviews;
- the announcement of new products or clinical trial data by our competitors;
- the announcement of regulatory applications, such as MSN’s and Teva’s respective ANDAs, seeking approval of generic versions of our marketed products;

- quarterly variations in our or our competitors' results of operations;
- changes in our relationships with our collaboration partners, including the termination or modification of our agreements, or other events or conflicts that may affect our collaboration partners' timing and willingness to develop, or if approved, commercialize our products and product candidates out-licensed to them;
- the announcement of an in-licensed product candidate or strategic acquisition;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- changes in earnings estimates or recommendations by securities analysts, or financial guidance from our management team, and any failure to achieve the operating results projected by securities analysts or by our management team;
- the entry into new financing arrangements;
- developments in the biotechnology, biopharmaceutical or pharmaceutical industry;
- sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;
- additions and departures of key personnel or board members;
- the disposition of any of our technologies or compounds; and
- general market, economic and political conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors, such as the impact of the COVID-19 pandemic on financial markets.

These and other factors could have material adverse impact on the market price of our common stock. In addition, the stock markets in general, and the markets for biotechnology and pharmaceutical stocks in particular, have historically experienced significant volatility that has often been unrelated or disproportionate to the operating performance of particular companies. Likewise, as a result of significant changes in U.S. or global political and economic conditions, including the effects of the COVID-19 pandemic, policies governing foreign trade and healthcare spending and delivery, or future potential U.S. federal government shutdowns, the financial markets could continue to experience significant volatility that could also continue to negatively impact the markets for biotechnology and pharmaceutical stocks. These broad market fluctuations have adversely affected and may in the future adversely affect the trading price of our common stock. Excessive volatility may continue for an extended period of time following the date of this report.

In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs and divert the attention of management, which could have a material adverse impact on our business, financial condition and results of operations.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent or deter attempts by our stockholders to replace or remove our current management, which could cause the market price of our common stock to decline.

Provisions in our corporate charter and bylaws may discourage, delay or prevent an acquisition of us, a change in control, or attempts by our stockholders to replace or remove members of our current Board of Directors. Because our Board of Directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a prohibition on actions by our stockholders by written consent;
- the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors; and
- advance notice requirements for director nominations and stockholder proposals.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

Not applicable.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

Not applicable.

Item 6. Exhibits

		Incorporation by Reference				
Exhibit Number	Exhibit Description	Form	File Number	Exhibit/ Appendix Reference	Filing Date	Filed Herewith
3.1	Restated Certificate of Incorporation of Exelixis, Inc.	10-Q	000-30235	3.1	8/5/2021	
3.2	Amended and Restated Bylaws of Exelixis, Inc.	8-K	000-30235	3.1	3/3/2021	
31.1	Certification of Principal Executive Officer Pursuant to Exchange Act Rules 13a-14(a) and Rule 15d-14(a)					X
31.2	Certification of Principal Financial Officer Pursuant to Exchange Act Rules 13a-14(a) and Rule 15d-14(a)					X
32.1‡	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350					X
101.INS	XBRL Instance Document	The XBRL instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X

‡ This certification accompanies this Quarterly Report on Form 10-Q, is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Exelixis, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of this Quarterly Report on Form 10-Q), irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements 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.

EXELIXIS, INC.

November 2, 2021	By:	/s/ Christopher J. Senner
Date		**Christopher J. Senner**
		Executive Vice President and Chief Financial Officer
		(Duly Authorized Officer and Principal Financial and Accounting Officer)

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO
EXCHANGE ACT RULES 13a-14(a) and 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael M. Morrissey, Ph.D., certify that:

1. I have reviewed this Form 10-Q of Exelixis, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/S/ Michael M. Morrissey, Ph.D.
Michael M. Morrissey, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 2, 2021

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
EXCHANGE ACT RULES 13a-14(a) and 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Christopher J. Senner, certify that:

1. I have reviewed this Form 10-Q of Exelixis, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

(c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

/S/ Christopher J. Senner

Christopher J. Senner
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

Date: November 2, 2021

Exhibit 32.1

**CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Michael M. Morrissey, Ph.D., the President and Chief Executive Officer of Exelixis, Inc. (the “Company”), and Christopher J. Senner, the Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company’s Quarterly Report on Form 10-Q for the period ended October 1, 2021, to which this Certification is attached as Exhibit 32.1 (the “Report”), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 2nd day of November 2021.

/S/ Michael M. Morrissey, Ph.D.	/S/ Christopher J. Senner
Michael M. Morrissey, Ph.D.	**Christopher J. Senner**
President and Chief Executive Officer (Principal Executive Officer)	Executive Vice President and Chief Financial Officer (Principal Financial Officer)