UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2020

OR

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

For the transition period from ________ to ________.

Commission file number 001-34655

AVEO PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3581650**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

30 Winter Street, Boston, Massachusetts 02108
(Address of principal executive offices) (Zip Code)

(857) 400-0101
(Registrant's telephone number, including area code)

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, $0.001 par value	AVEO	Nasdaq Capital Market

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

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

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

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

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

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

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on November 6, 2020: 28,809,249

AVEO PHARMACEUTICALS, INC.

FORM 10-Q
FOR THE QUARTER ENDED SEPTEMBER 30, 2020

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AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(In thousands, except par value amounts)
(Unaudited)

	September 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 39,848	$ 29,785
Marketable securities	28,996	17,960
Accounts receivable	1,052	1,631
Clinical trial retainers	476	589
Other prepaid expenses and other current assets	1,270	635
Total current assets	71,642	50,600
Property and equipment, net	210	—
Operating lease right-of-use asset	1,012	—
Other assets	158	—
Total assets	$ 73,022	$ 50,600
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,999	$ 1,466
Accrued clinical trial costs and contract research	5,925	5,680
Other accrued liabilities	3,411	2,336
Operating lease liability	436	—
Loans payable, net of discount	—	9,569
Deferred revenue	1,974	1,974
Deferred research and development reimbursements	240	93
PIPE Warrant liability (Note 7)	1,913	—
Other liabilities (Note 6)	790	—
Total current liabilities	16,688	21,118
Loans payable, net of current portion and discount	13,617	6,197
Deferred revenue	1,072	2,552
PIPE Warrant liability (Note 7)	—	5,097
Operating lease liability, non-current	379	—
Other liabilities (Note 6)	1,043	790
Total liabilities	32,799	35,754
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized at September 30, 2020 and December 31, 2019; no shares issued and outstanding at each of September 30, 2020 and December 31, 2019	—	—
Common stock, $.001 par value: 50,000 shares authorized at September 30, 2020 and December 31, 2019; 25,808 shares issued and outstanding at September 30, 2020 and 16,081 issued and outstanding at December 31, 2019	26	16
Additional paid-in capital	649,897	600,451
Accumulated other comprehensive income	1	—
Accumulated deficit	(609,701)	(585,621)
Total stockholders' equity	40,223	14,846
Total liabilities and stockholders' equity	$ 73,022	$ 50,600

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(In thousands, except per share amounts)
(Unaudited)

	Three Months Ended September 30, 2020	Three Months Ended September 30, 2019	Nine Months Ended September 30, 2020	Nine Months Ended September 30, 2019
Revenues:				
Collaboration and licensing revenue	$ 3,293	$ 25,494	$ 4,280	$ 27,441
Partnership royalties	307	223	853	590
	3,600	25,717	5,133	28,031
Operating expenses:				
Research and development	5,860	3,983	18,105	13,446
Selling, general and administrative	5,800	2,884	13,209	8,325
	11,660	6,867	31,314	21,771
Income (loss) from operations	(8,060)	18,850	(26,181)	6,260
Other income (expense), net:				
Interest expense, net	(419)	(467)	(1,083)	(1,482)
Change in fair value of PIPE Warrant liability	86	(1,954)	3,184	9,071
Other income (expense), net	(333)	(2,421)	2,101	7,589
Net income (loss)	$ (8,393)	$ 16,429	$ (24,080)	$ 13,849
Basic net income (loss) per share				
Net income (loss) per share	$ (0.33)	$ 1.02	$ (1.22)	$ 0.92
Weighted average number of common shares outstanding	25,808	16,074	19,773	15,079
Diluted net income (loss) per share				
Net income (loss) per share	$ (0.33)	$ 1.02	$ (1.22)	$ 0.92
Weighted average number of common shares and dilutive common share equivalents outstanding	25,808	16,083	19,773	15,129

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Income (Loss)
(In thousands)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Net income (loss)	$ (8,393)	$ 16,429	$ (24,080)	$ 13,849
Other comprehensive income (loss):				
Unrealized gain (loss) on available-for-sale securities	2	(1)	1	(1)
Comprehensive income (loss)	$ (8,391)	$ 16,428	$ (24,079)	$ 13,848

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(In thousands)
(Unaudited)

	Common Shares					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2019	16,081	$ 16	$ 600,451	$ —	$ (585,621)	$ 14,846
Stock-based compensation expense related to equity- classified awards	—	—	543	—	—	543
Net loss	—	—	—	—	(8,381)	(8,381)
Balance at March 31, 2020	16,081	$ 16	$ 600,994	$ —	$ (594,002)	$ 7,008
Issuance of common stock in a public offering, excluding to related parties (net of issuance costs of $3.3 million)	5,221	5	24,074	—	—	24,079
Issuance of common stock in a public offering, to related parties	4,504	5	23,639	—	—	23,644
Stock-based compensation expense related to equity-classified awards	—	—	578	—	—	578
Issuance of common stock under employee stock purchase plan	2	—	18	—	—	18
Change in unrealized gain (loss) on investments	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	(7,306)	(7,306)
Balance at June 30, 2020	25,808	$ 26	$ 649,303	$ (1)	$ (601,308)	$ 48,020
Stock-based compensation expense related to equity-classified awards	—	—	594	—	—	594
Change in unrealized gain (loss) on investments	—	—	—	2	—	2
Net loss	—	—	—	—	(8,393)	(8,393)
Balance at September 30, 2020	**25,808**	**$ 26**	**$ 649,897**	**$ 1**	**$ (609,701)**	**$ 40,223**

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity (Deficit)
(In thousands)
(Unaudited)

	Common Shares					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2018	12,648	$ 13	$ 567,768	$ 1	$ (595,009)	$ (27,227)
Issuance of common stock from the SVB Leerink sales agreement (net of issuance costs of $0.2 million)	1,252	1	7,511	—	—	7,512
Stock-based compensation expense related to equity-classified awards	—	—	584	—	—	584
Net income	—	—	—	—	555	555
Balance at March 31, 2019	13,900	$ 14	$ 575,863	$ 1	$ (594,454)	$ (18,576)
Issuance of common stock and warrants in a public offering, excluding to related parties (net of issuance costs of $2.3 million)	1,739	2	17,765	—	—	17,767
Issuance of common stock and warrants in a public offering, to related parties	435	—	5,000	—	—	5,000
Stock-based compensation expense related to equity-classified awards	—	—	584	—	—	584
Exercise of stock options	—	—	3	—	—	3
Net loss	—	—	—	—	(3,135)	(3,135)
Balance at June 30, 2019	16,074	$ 16	$ 599,215	$ 1	$ (597,589)	$ 1,643
Stock-based compensation expense related to equity-classified awards	—	—	686	—	—	686
Change in unrealized gain (loss) on investments	—	—	—	(1)	—	(1)
Net income	—	—	—	—	16,429	16,429
Balance at September 30, 2019	**16,074**	**$ 16**	**$ 599,901**	**$ —**	**$ (581,160)**	**$ 18,757**

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(In thousands)
(Unaudited)

	Nine Months Ended September 30, 2020	Nine Months Ended September 30, 2019
Operating activities		
Net income (loss)	$ (24,080)	$ 13,849
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	9	—
Stock-based compensation	1,715	1,854
Non-cash interest expense	314	445
Non-cash change in fair value of PIPE Warrant liability	(3,184)	(9,071)
Amortization of premium and discount on investments	(99)	(1)
Changes in operating assets and liabilities:		
Accounts receivable	579	1,936
Prepaid expenses and other current assets	(522)	(534)
Operating lease right-of-use asset	(1,170)	—
Accounts payable	533	(1,316)
Accrued contract research	245	(1,155)
Other accrued liabilities	1,075	(893)
Operating lease liability	436	—
Deferred revenue	(1,480)	(441)
Deferred research and development reimbursements	147	(221)
Operating lease liability, non-current	379	—
Net cash (used in) provided by operating activities	(25,103)	4,452
Investing activities		
Purchases of marketable securities	(36,133)	—
Proceeds from maturities and sales of marketable securities	25,200	—
Purchases of property and equipment	(219)	—
Net cash used in investing activities	(11,152)	—
Financing activities		
Proceeds from issuance of common stock and warrants, net of issuance costs	24,079	25,279
Proceeds from issuance of common stock and warrants to related parties	23,644	5,000
Proceed from issuance of loan payable	5,329	
Proceeds from issuance of common stock for stock-based compensation arrangements	18	3
Payment of principal of loan payable	(6,497)	(1,507)
Payment of debt issuance costs	(255)	
Net cash provided by financing activities	46,318	28,775
Net increase in cash and cash equivalents	10,063	33,227
Cash and cash equivalents at beginning of period	29,785	24,427
Cash and cash equivalents at end of period	$ 39,848	$ 57,654
Supplemental cash flow information		
Cash paid for interest	$ 971	$ 1,539
Right-of-use asset obtained in exchange for operating lease liabilities	$ 1,225	$ —

See accompanying notes.

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. The Company's strategy is to focus its resources toward development and commercialization of its product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies.

The Company's lead candidate is tivozanib (FOTIVDA), a vascular endothelial growth factor receptor tyrosine kinase inhibitor. FOTIVDA is approved through the Company's development partner EUSA Pharma (UK) Limited ("EUSA") in the European Union, the United Kingdom, Norway, New Zealand and Iceland for the first-line treatment of adult patients with advanced renal cell carcinoma ("RCC"). The Company is working to develop and potentially commercialize tivozanib in the U.S. as a treatment for RCC and hepatocellular carcinoma, or HCC. In March 2020, the Company submitted an application for marketing approval ("NDA") to the U.S. Food and Drug Administration ("FDA") for tivozanib as a treatment for relapsed or refractory RCC. In June 2020, the FDA accepted the NDA for substantive review and assigned it a Prescription Drug User Fee Act ("PDUFA") target date of March 31, 2021. The Company completed an application orientation meeting with the FDA on May 14, 2020 and a mid-cycle review meeting on July 31, 2020. The FDA has conditionally accepted the Company's proposed brand name, FOTIVDA, for tivozanib in the United States. The FDA has also notified the Company that it does not currently plan to convene an Oncologic Drugs Advisory Committee meeting in connection with its NDA review. In addition to developing tivozanib as a potential monotherapy, and based on tivozanib's demonstrated anti-tumor activity and tolerability profile, the Company is studying tivozanib in combination with immune checkpoint inhibitors for the treatment of RCC and HCC in phase 2 clinical trials.

The Company's pipeline of product candidates also includes ficlatuzumab, a hepatocyte growth factor ("HGF") inhibitory antibody. The Company has previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck ("HNSCC"), acute myeloid leukemia ("AML") and pancreatic cancer. The Company is currently conducting a randomized phase 2 confirmatory study of ficlatuzumab for the potential treatment of HNSCC. The Company's earlier stage pipeline under development includes AV-203, an anti-ErbB3 monoclonal antibody, as a potential oncology treatment; AV-380, a humanized IgG1 inhibitory monoclonal antibody targeting growth differentiation factor 15 ("GDF15"), a divergent member of the TGF-ß family, for the potential treatment of cancer cachexia; and AV-353, which targets the Notch 3 pathway, as a potential oncology treatment.

The Company is subject to a number of risks, including the need for substantial additional capital to continue its development programs and to fulfill its planned operating goals. In particular, the Company's currently planned operating and capital requirements include the need for substantial working capital to support the development and commercialization activities for its lead product candidate, tivozanib.

As used throughout these condensed consolidated financial statements, the terms "AVEO," and the "Company" refer to the business of AVEO Pharmaceuticals, Inc. and its three wholly-owned subsidiaries, AVEO Pharma Limited, AVEO Pharma (Ireland) Limited and AVEO Securities Corporation.

Liquidity and Going Concern

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through September 30, 2020, the Company has financed its operations primarily through private placements and public offerings of its common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations.

The Company has incurred recurring losses and cash outflows from operations since its inception, including an accumulated deficit of $609.7 million as of September 30, 2020. The Company expects to continue to generate operating losses for the foreseeable future. As of November 9, 2020, the date of issuance of these unaudited condensed consolidated financial statements, the Company expects that its cash, cash equivalents and marketable securities of $68.8 million as of September 30, 2020 will not be sufficient to fund its current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q. This condition raises substantial doubt about the Company's ability to continue as a going concern.

The Company's plans to address this condition include pursuing one or more of the following options to secure additional funding, none of which can be guaranteed or are entirely within the Company's control:

- Earn royalty payments pursuant to the Company's license agreement (the "EUSA Agreement") with EUSA for EUSA's sales of tivozanib in its territory.
- Earn milestone payments pursuant to the collaboration and license agreements described in Note 4 or restructure / monetize existing potential milestone and/or royalty payments under those collaboration and license agreements.
- Raise funding through the possible additional sale of the Company's common stock, including public or private equity financings and / or sales of the Company's common stock under the Leerink Sales Agreement, as defined and discussed in Note 7.
- Drawdown potential future borrowings pursuant to the loan agreement with Hercules Funding III, LLC and Hercules Capital, Inc. (collectively "Hercules"), subject to the satisfaction of the conditions to future borrowing.
- Partner a portion or all rights to the Company's portfolio candidates to secure potential additional non-dilutive funds.

Pursuant to the EUSA Agreement, the Company is entitled to receive up to an additional $4.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France and Italy, and an additional $2.0 million milestone payment for the grant of marketing approval, if any, in three of the licensed countries outside of the European Union (the "EU"), as mutually agreed by the parties. These milestone payments are subject to the 30% sublicense fee payable to Kyowa Kirin Co. (formerly Kirin Brewery Co., Ltd.) ("KKC") pursuant to the Company's license agreement with KKC (the "KKC Agreement"). The Company is also eligible to receive additional research and development reimbursement payments from EUSA if EUSA elects to opt-in to the TIVO-3 study.Refer to Note 4 "*Collaborations and License Agreements - InLicense Agreements – Kyowa Kirin Co. (KKC)*" for further details.

The Company is also eligible, at its option, to borrow up to an additional $20.0 million under the amendment to the loan agreement with Hercules, subject to certain terms and conditions including FDA approval of FOTIVDA and, if approved, the Company's net product revenues from sales of FOTIVDA reaching $20.0 million within a specified time frame. There can be no assurance, however, that the FDA will approve FOTIVDA or that the other conditions to the funding of such loan amounts will be satisfied. Refer to Note 6 *"Hercules Loan Facility"* for further details.

However, there can be no assurance that the Company will receive cash proceeds from any of these potential resources or to the extent cash proceeds are received such proceeds would be sufficient to support the Company's current operating plan for more than twelve months from the date of filing this Quarterly Report on Form 10-Q.

When substantial doubt exists after performing the initial valuation under Subtopic 205-40, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued.

Under ASC 205-40, the future receipt of potential funding from the Company's collaborators and funding that is contingent on FDA approval of FOTIVDA, such as the potential future borrowings pursuant to the loan agreement with Hercules and product revenues from the sales of FOTIVDA, cannot be considered probable at this time because none of the Company's current plans have been finalized at the time of filing this Quarterly Report on Form 10-Q and the implementation of any such plan is not probable of being effectively implemented as none of the plans are entirely within the Company's control. Accordingly, substantial doubt is deemed to exist about the Company's ability to continue as a going concern within one year after the date these financial statements are issued.

If the Company is unable to obtain sufficient capital to continue to advance its programs, the Company would be forced to delay, reduce or eliminate its research and development programs and any future commercialization efforts.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

(2) Basis of Presentation

These condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, AVEO Pharma Limited, AVEO Pharma (Ireland) Limited and AVEO Securities Corporation. The Company has eliminated all significant intercompany accounts and transactions in consolidation.

The accompanying condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") for interim financial information and with the instructions to Form 10-Q and Article 8 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In the opinion of management, all adjustments, consisting of normal recurring accruals and revisions of estimates, considered necessary for a fair presentation of the condensed consolidated financial statements have been included. Interim results for the three and nine months ended September 30, 2020 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2020 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at September 30, 2020, and for the three months and nine months ended September 30, 2020 and 2019, is unaudited, and the condensed consolidated balance sheet amounts and related footnotes as of December 31, 2019 have been derived from the Company's audited financial statements. For further information, refer to the consolidated financial statements and accompanying footnotes included in the Company's annual report on Form 10-K for the fiscal year ended December 31, 2019, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 16, 2020.

Effective as of 5:00 p.m. Eastern Time on February 19, 2020, the Company effected a 1-for-10 reverse stock split of its common stock. All references to shares of common stock outstanding and per share amounts in these condensed consolidated financial statements and the notes to the condensed consolidated financial statements have been restated to reflect the reverse stock split on a retroactive basis. Refer to Note 7, "*Common Stock – Reverse Stock Split – February 2020*" for further details.

(3) Significant Accounting Policies

Revenue Recognition

The Company's revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple promised goods and services, which may include (i) licenses, or options to obtain licenses, to the Company's technology, (ii) research and development activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Collaboration Arrangements Within the Scope of ASC 808, Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and are therefore within the scope of ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are deemed to be within the scope of ASC 808, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company's policy is generally to recognize amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction in research and development expense.

Arrangements Within the Scope of ASC 606, Revenue from Contracts with Customers

Under ASC 606, the Company recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration which the Company determines it expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligation(s). As part of the accounting for these arrangements, the Company must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Once a contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within the contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an output or input method.

Licenses of intellectual property: The terms of the Company's license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of the Company's ongoing activities. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from the portion of the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises (that is, for licenses that are not distinct from other promised goods and services in an arrangement), the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and development funding: Arrangements that include payment for research and development services are generally considered to have variable consideration. If and when the Company assesses the payment for these services is no longer subject to the constraint on variable consideration, the related revenue is included in the transaction price.

Milestone payments: At the inception of each arrangement that includes non-refundable payments for contingent milestones, including preclinical research and development, clinical development and regulatory, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of the achievement of contingent milestones and the likelihood of a significant reversal of such milestone revenue, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and licensing revenue in the period of adjustment. This quarterly assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

The following table summarizes the total revenues earned in the three months and nine months ended September 30, 2020 and 2019, respectively, by partner (in thousands). Refer to Note 4, *"Collaborations and License Agreements"* regarding specific details.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
KKC	$ 2,800	$ 25,000	$ 2,800	$ 25,000
EUSA	800	717	2,333	3,031
Total	$ 3,600	$ 25,717	$ 5,133	$ 28,031

Leases

The Company adopted ASU 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), effective January 1, 2019 using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, *Leases*. In connection with the adoption of ASU 2016-02, the Company elected the package of practical expedients permitted under the transition guidance within the new standard, which does not require the reassessment of the following: (i) whether existing or expired arrangements are or contain a lease, (ii) the lease classification of existing or expired leases, and (iii) whether previous initial direct costs would qualify for capitalization under the new lease standard. The Company made an accounting policy election not to recognize right-of-use assets or related lease liabilities with a lease term of twelve months or less in its Consolidated Balance Sheet. Such short-term lease payments are recorded in its Consolidated Statements of Operations in the period in which the obligation for those payments was incurred.

As of the date of initial application of ASU 2016-02, the Company's lease arrangement for its former corporate headquarters at One Broadway, Cambridge, Massachusetts was cancellable within 30 days' notice to its landlord and excluded any extension incentives or disincentives to renew for an extended period of time. In addition, the Company has drug storage arrangements with multiple storage providers that are cancellable at any time without penalty to the Company. The Company recognized short-term operating lease expense in its Consolidated Statements of Operations of approximately $0.2 million in each of the three months ended September 30, 2020 and 2019, and $0.7 million and $0.6 million in the nine months ended September 30, 2020 and 2019, respectively.

Application of ASC 842 policy elections to leases post adoption

The Company has made certain accounting policy elections to apply to its leases executed post adoption of ASU 2016-02 , or subsequent to January 1, 2019, as further described below.

In accordance with ASC 842, components of a lease should be split into three categories: lease components, non-lease components, and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components. The Company made an accounting policy election to combine lease and non-lease components as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

ASC 842 allows for the use of judgment in determining whether the assumed lease term is for a major part of the remaining economic life of the underlying asset and whether the present value of lease payments represents substantially all of the fair value of the underlying asset. The Company applies the bright line thresholds referenced in ASC 842-10-55-2 to assist in evaluating leases for appropriate classification.

30 Winter Street Lease

On March 5, 2020, the Company entered into a sublease agreement for office space located at 30 Winter Street in Boston, Massachusetts (the "Winter Street Sublease") to relocate the Company's corporate headquarters previously located at One Broadway in Cambridge, Massachusetts. Under the terms of the Winter Street Sublease, the Company leases 10,158 square feet of office space for $47.00 per square foot, or approximately $0.5 million per year in base rent subject to certain operating expenses, taxes and annual base rent increases of approximately 3%. The Winter Street Sublease commenced when the space became available for use by the Company on March 24, 2020 and will continue until its expiration on November 30, 2022. Upon commencement of the Winter Street Sublease, the Company paid a security deposit, in the amount of $0.3 million, which is subject to certain reductions to be applied to future base rent payments provided that no event of default has occurred in the preceding twelve months.

The Company is accounting for the Winter Street Sublease under ASC 842 using its initial 2.7-year term through November 30, 2022. In applying ASC 842, the Company classified the Winter Street Sublease as an operating lease and recorded a right-of-use asset of approximately $1.2 million and a lease liability of approximately $1.0 million upon the effective lease commencement date. In calculating the lease liability, the Company used the present value of all future lease payments using an incremental borrowing rate of 7.58%. The Company is recognizing rent expense on a straight-line basis throughout the remaining term of the lease. In the nine months ended September 30, 2020, the Company recognized $0.2 million in rent expense.

In connection with the execution of the Winter Street Sublease, the Company also entered into a Purchase Agreement for furniture (the "Furniture Purchase Agreement") located on the premises upon the lease commencement. Upon execution of the Furniture Purchase Agreement, the Company paid the $0.1 million purchase price and recorded the furniture acquisition as property and equipment, net. The Company is recognizing depreciation using the straight-line method over the estimated useful life of 7 years.

As of September 30, 2020, future minimum lease payments under the Company's Winter Street Sublease are as follows (amounts in thousands):

Year Ending December 31:		
2020 (remaining 3 months)		119
2021		385
2022		328
Total lease payments		832
Less imputed interest		(17)
Total operating lease liabilities	$	815

Research and Development Expenses

Research and development expenses are charged to expense as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including (i) internal costs for salaries, bonuses, benefits, stock-based compensation, research-related overhead, and allocated expenses for facilities and information technology, and (ii) external costs for clinical trials, drug manufacturing and distribution, manufacturing costs for pre-launch inventory that did not qualify for capitalization, preclinical studies, upfront license payments, milestones and sublicense fees related to in-licensed products and technology, consultants and other contracted services.

Warrants Issued in Connection with Private Placement

In May 2016, the Company issued warrants to purchase an aggregate of 1,764,242 shares of common stock in connection with a private placement financing and recorded the warrants as a liability (the "PIPE Warrants"). The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. As of September 30, 2020, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding. Refer to Note 7, "*Common Stock—Private Placement – May 2016"* for further discussion of the private placement financing.

The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, *Distinguishing Liabilities from Equity* requires that these warrants be classified as a liability and not as equity. Accordingly, the Company recorded a warrant liability in the amount of approximately $9.3 million upon issuance of the PIPE Warrants. The fair value of these warrants has been determined using the Black-Scholes pricing model. These warrants are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net until the earlier of their exercise or expiration or upon the completion of a liquidation event. Upon exercise, the PIPE Warrants are subject to revaluation just prior to the date of the warrant exercise and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net and the corresponding reduction in the PIPE Warrant liability is recorded as additional paid-in capital in the Balance Sheet as a component of stockholder's equity.

The Company recorded a non-cash gain of approximately $0.1 million in the three months ended September 30, 2020 in its Statement of Operations attributable to the decrease in the fair value of the warrant liability that resulted from a decrease in the Company's stock volatility rate and a shorter remaining term as the PIPE Warrants approach their expiration in May 2021, partially offset by a higher Company stock price as of September 30, 2020 relative to prior periods.

The Company recorded a non-cash gain of approximately $3.2 million in the nine months ended September 30, 2020 in its Statement of Operations attributable to the decrease in the fair value of the warrant liability that resulted from a lower Company stock price as of September 30, 2020 relative to prior periods, a decrease in the Company's stock volatility rate and a shorter remaining term as the PIPE Warrants approach their expiration in May 2021.

The Company recorded a non-cash loss of approximately $2.0 million in the three months ended September 30, 2019 in its Statement of Operations attributable to the increase in the fair value of the warrant liability that principally resulted from a higher Company stock price as of September 30, 2019 relative to prior periods. The Company recorded a non-cash gain of approximately $9.1 million in the nine months ended September 30, 2019 in its Statement of Operations attributable to the decrease in the fair value of the warrant liability that principally resulted from a lower Company stock price as of September 30, 2019 relative to prior periods.

The following table rolls forward the fair value of the Company's PIPE Warrant liability, the fair value of which is determined by Level 3 inputs for the nine months ended September 30, 2020 (in thousands):

Fair value at January 1, 2020	$	5,097
Decrease in fair value		(2,648)
Fair value at March 31, 2020	$	2,449
Decrease in fair value		(450)
Fair value at June 30, 2020	$	1,999
Decrease in fair value		(86)
Fair value at September 30, 2020	$	1,913

The key assumptions used to value the PIPE Warrants in the three months and nine months ended September 30, 2020 were as follows:

	December 31, 2019	March 31, 2020	June 30, 2020	September 30, 2020
Expected price volatility	133.07%	153.37%	108.20%	103.29%
Expected term (in years)	1.50	1.25	1.00	0.75
Risk-free interest rates	1.59%	0.17%	0.16%	0.12%
Stock price	$ 6.20	$ 3.62	$ 5.15	$ 5.94
Dividend yield	—	—	—	—

The key assumptions used to value the PIPE Warrants in the three months and nine months ended September 30, 2019 were as follows:

	December 31, 2018	March 31, 2019	June 30, 2019	September 30, 2019
Expected price volatility	82.64%	111.99%	113.86%	119.11%
Expected term (in years)	2.50	2.25	2.00	1.75
Risk-free interest rates	2.47%	2.27%	1.75%	1.63%
Stock price	$ 16.00	$ 8.20	$ 6.70	$ 8.40
Dividend yield	—	—	—	—

Cash, Cash Equivalents and Marketable Securities

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase and an investment in a U.S. government money market fund to be cash equivalents. Changes in the balance of cash and cash equivalents may be affected by changes in investment portfolio maturities, as well as actual cash disbursements to fund operations.

The Company's cash is deposited in highly-rated financial institutions in the United States. The Company invests in U.S. government money market funds, high-grade, short-term commercial paper, corporate bonds and other U.S. government agency securities, which management believes are subject to minimal credit and market risk. The carrying values of the Company's cash and cash equivalents approximate fair value due to their short-term maturities.

The Company does not have any restricted cash balances.

Marketable securities consist primarily of investments which have expected average maturity dates in excess of three months. The Company invests in high-grade corporate obligations, including commercial paper, and U.S. government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the condensed consolidated balance sheets.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive income or loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. The cost of marketable securities is adjusted for amortization of premiums and accretion of discounts, with such amortization and accretion recorded as a component of interest expense, net. Realized gains and losses are determined on the specific identification method. Unrealized gains and losses are included in other comprehensive loss until realized, at which point they would be recorded as a component of interest expense, net.

Below is a summary of cash, cash equivalents and marketable securities at September 30, 2020 and December 31, 2019 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
September 30, 2020				
Cash and cash equivalents:				
Cash and money market funds	$ 39,848	$ —	$ —	$ 39,848
Total cash and cash equivalents	**39,848**	—	—	**39,848**
Marketable securities:				
Corporate debt securities due within 1 year	$ 9,998	$ —	$ —	$ 9,998
U.S. government agency securities due within 1 year	18,997	—	1	18,998
Total marketable securities	28,995	—	1	28,996
Total cash, cash equivalents and marketable securities	**$ 68,843**	**$ —**	**$ 1**	**$ 68,844**
December 31, 2019				
Cash and cash equivalents:				
Cash and money market funds	$ 25,278	$ —	$ —	$ 25,278
Corporate debt securities	4,507	—	—	4,507
Total cash and cash equivalents	**29,785**	—	—	**29,785**
Marketable securities:				
Corporate debt securities due within 1 year	$ 17,960	$ —	$ —	$ 17,960
Total marketable securities	17,960	—	—	17,960
Total cash, cash equivalents and marketable securities	**$ 47,745**	**$ —**	**$ —**	**$ 47,745**

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents, marketable securities and accounts receivable. The Company maintains deposits in highly-rated, federally-insured financial institutions in excess of federally insured limits. The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the high credit quality standards outlined in the Company's investment policy. This policy also limits the amount of credit exposure to any one issue or type of instrument.

The Company's accounts receivable primarily consists of amounts due to the Company from licensees and collaborators. The Company has not experienced any material losses related to accounts receivable from individual licensees or collaborators.

Fair Value Measurements

The fair value of the Company's financial assets and liabilities reflects the Company's estimate of amounts that it would have received in connection with the sale of the assets or paid in connection with the transfer of the liabilities in an orderly transaction between market participants at the measurement date. In connection with measuring the fair value of its assets and liabilities, the Company seeks to maximize the use of observable inputs (market data obtained from sources independent from the Company) and to minimize the use of unobservable inputs (the Company's assumptions about how market participants would price assets and liabilities). The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used in order to value the assets and liabilities:

Level 1: Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2: Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3: Unobservable inputs based on the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs.

As of September 30, 2020, the Company had financial assets valued based on Level 1 inputs consisting of cash and cash equivalents in U.S. government money market funds, and had financial assets based on Level 2 inputs consisting of high-grade debt securities, including commercial paper, and government agency securities. During the three months and nine months ended September 30, 2020, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of September 30, 2020, the Company's financial liability that was recorded at fair value consisted of the PIPE Warrant liability.

The fair value of the Company's loans payable at September 30, 2020 and December 31, 2019 approximates its carrying value, computed pursuant to a discounted cash flow technique using a market interest rate and is considered a Level 3 fair value measurement. The effective interest rate, which reflects the current market rate, considers the fair value of the warrants issued in connection with the loan, loan issuance costs and the deferred financing charge.

The following table summarizes the financial assets and liabilities measured at fair value on a recurring basis at September 30, 2020 and December 31, 2019 (in thousands):

	Fair Value Measurements as of September 30, 2020			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$ 39,848	$ —	$ —	$ 39,848
Total cash and cash equivalents	$ 39,848	$ —	$ —	$ 39,848
Marketable securities:				
Corporate debt securities due within 1 year	$ —	$ 9,998	$ —	$ 9,998
U.S. government agency securities due within 1 year	—	18,998	—	18,998
Total marketable securities	$ —	$ 28,996	$ —	$ 28,996
Total cash, cash equivalents and marketable securities	**$ 39,848**	**$ 28,996**	**$ —**	**$ 68,844**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 1,913**	**$ 1,913**

	Fair Value Measurements as of December 31, 2019			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$ 25,278	$ —	$ —	$ 25,278
Corporate debt securities	—	4,507	—	4,507
Total cash and cash equivalents	$ 25,278	$ 4,507	$ —	$ 29,785
Marketable securities:				
Corporate debt securities due within 1 year	$ —	$ 17,960	$ —	$ 17,960
Total marketable securities	$ —	$ 17,960	$ —	$ 17,960
Total cash, cash equivalents and marketable securities	**$ 25,278**	**$ 22,467**	**$ —**	**$ 47,745**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 5,097**	**$ 5,097**

Basic and Diluted Net Income (Loss) per Common Share

Basic net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period plus additional weighted-average common equivalent shares outstanding during the period when the effect is dilutive.

For each of the three months and nine months ended September 30, 2020, diluted net loss per share is the same as basic net loss per share as the inclusion of weighted-average shares of common stock issuable upon the exercise of outstanding stock options and warrants would be anti-dilutive. In each of the three months and nine months ended September 30, 2020, the average market prices of the Company's common stock were below the exercise prices of $10.00 and $12.50 per share for the PIPE Warrants and Offering Warrants (as defined in Note 7 – *Common Stock – Public Offering – April 2019* below), respectively.

For each of the three months and nine months ended September 30, 2019, diluted net income per share (i) includes common equivalent shares issuable upon the exercise of in-the-money stock options, as determined using the treasury stock method, as the average market prices of the Company's common stock during the respective periods exceeded the exercise prices of certain stock options, and (ii) excludes the incremental common shares issuable upon the exercise of the PIPE Warrants, Offering Warrants, Settlement Warrants (as defined in Note 7 – *Common Stock – Settlement Warrants* below) and out-of-the money stock options as their effect would be anti-dilutive. In each of the three months and nine months ended September 30, 2019, the average market prices of the Company's common stock were below the exercise prices of $10.00, $12.50 and $30.00 per share for the PIPE Warrants, Offering Warrants and Settlement Warrants, respectively. All 200,000 Settlement Warrants expired on July 15, 2019 as none of these warrants had been exercised. Refer to Note 7, "*Common Stock—Private Placement – May 2016, - Public Offering – April 2019 and - Settlement Warrants"* for further discussion of these warrants.

The following table summarizes the computation of basic and diluted net income (loss) per share for the three months and nine months ended September 30, 2020 and 2019, respectively (in thousands except per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Net income (loss) attributable to AVEO common stockholders	$ (8,393)	$ 16,429	$ (24,080)	$ 13,849
Weighted-average shares of common stock outstanding	25,808	16,074	19,773	15,079
Dilutive securities:				
Weighted-average number of common shares outstanding and dilutive share equivalents outstanding	—	9	—	50
Weighted-average number of common shares outstanding and dilutive share equivalents outstanding	25,808	16,083	19,773	15,129
Basic net income (loss) per share	$ (0.33)	$ 1.02	$ (1.22)	$ 0.92
Diluted net income (loss) per share	$ (0.33)	$ 1.02	$ (1.22)	$ 0.92

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as the effect would have been anti-dilutive for the three months and nine months ended September 30, 2020 and 2019, respectively (in thousands):

	Outstanding at September 30,	
	2020	2019
Options outstanding	1,691	588
Offering Warrants outstanding	2,500	2,500
PIPE Warrants outstanding	1,684	1,684
Total	5,875	4,772

Stock-Based Compensation

Under the Company's stock-based compensation programs, the Company periodically grants stock options and restricted stock to employees, directors and nonemployee consultants. The Company also issues shares under an employee stock purchase plan. The fair value of each award is recognized in the Company's statements of operations over the requisite service period for such award.

Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. The Company uses the Black-Scholes option pricing model to value its stock option awards without market conditions, which requires the Company to make certain assumptions regarding the expected volatility of its common stock price, the expected term of the option grants, the risk-free interest rate and the dividend yield with respect to its common stock. The Company calculates volatility using its historical stock price data. Due to the lack of the Company's own historical data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the Company's stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends.

The fair value of equity-classified awards to employees and directors is measured at fair value on the date the award is granted. During the three and nine months ended September 30, 2020 and 2019, the Company recorded the following stock-based compensation expense (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Research and development	$ 123	$ 200	$ 363	$ 538
General and administrative	471	486	1,352	1,316
Total	$ 594	$ 686	$ 1,715	$ 1,854

Stock-based compensation expense is allocated to research and development and general and administrative expense based upon the department of the employee to whom each award was granted. No related tax benefits of the stock-based compensation expense have been recognized.

Income Taxes

The Company provides for income taxes using the asset-liability method. Under this method, deferred tax assets and liabilities are recognized based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company calculates its provision for income taxes on ordinary income based on its projected annual tax rate for the year. Uncertain tax positions are recognized if the position is more-likely-than-not to be sustained upon examination by a tax authority. Unrecognized tax benefits represent tax positions for which reserves have been established. As of September 30, 2020, the Company is forecasting an effective tax rate of 0% for the year ending December 31, 2020. The Company maintains a full valuation allowance on all deferred tax assets.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment principally in the United States. As of September 30, 2020, the Company had no net assets located outside of the United States.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, the assessment of the Company's ability to continue as a going concern, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, clinical trial costs and contract research accruals, measurement of the PIPE Warrant liability, measurement of stock-based compensation, measurement of right-of-use assets and lease liabilities, and estimates of the Company's capital requirements over the next twelve months from the date of issuance of the condensed consolidated financial statements. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in the Company's disclosures in the period in which they become known. Actual results could differ from those estimates if past experience or other assumptions do not turn out to be substantially accurate.

Recently Adopted Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued ASU 2016-13, *Measurement of Credit Losses on Financial Instruments,* ("ASU 2016-13"). This standard requires that for most financial assets, losses be based on an expected loss approach which includes estimates of losses over the life of exposure that considers historical, current and forecasted information. Expanded disclosures related to the methods used to estimate the losses as well as a specific disaggregation of balances for financial assets are also required. The targeted transition relief standard allows filers an option to irrevocably elect the fair value option of ASC 825-10, Financial Instruments-Overall, applied on an instrument-by-instrument basis for eligible instruments. The Company adopted ASU 2016-13 effective January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies the disclosure requirements for fair value measurements. The Company adopted ASU 2018-13 effective January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective beginning January 1, 2021. The Company is assessing the impact ASU 2019-12 will have on its consolidated financial statements.

(4) Collaborations and License Agreements

Out-License and Collaboration Agreements

AstraZeneca

In December 2018, the Company entered into a clinical supply agreement (the "AstraZeneca Agreement") with a wholly-owned subsidiary of AstraZeneca PLC ("AstraZeneca") to evaluate the safety and efficacy of AstraZeneca's IMFINZI (durvalumab), a human monoclonal antibody directed against programmed death-ligand 1 (PD-L1), in combination with tivozanib as a first-line treatment for patients with advanced, unresectable HCC in an open-label, multi-center, randomized phase 1b/2 clinical trial (the "DEDUCTIVE trial"). The Company serves as the study sponsor; each party contributes the clinical supply of its study drug; key decisions are made by both parties by consensus; and external study costs are otherwise shared equally.

The Company is accounting for the joint development activities under the AstraZeneca Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and AstraZeneca are active participants in the oversight of the DEDUCTIVE trial via their participation on a joint steering committee and are exposed to significant risk and rewards in connection with the activity based on their obligation to share in the costs. AstraZeneca does not meet the definition of a customer, thus the joint development activities under the AstraZeneca Agreement are not accounted for under ASC 606.

Payments from AstraZeneca with respect to its share of the external costs for the DEDUCTIVE trial incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities that is not representative of a vendor-customer relationship.

The Company records reimbursements from AstraZeneca for external study costs as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the AstraZeneca Agreement, the Company's research and development expenses were reduced by approximately $0.2 million in the each of the three months ended September 30, 2020 and 2019, respectively, and by approximately $0.8 million and $0.3 million in the nine months ended September 30, 2020 and 2019, respectively. The amount due to the Company from AstraZeneca pursuant to the cost-sharing provision was approximately $0.4 million as of September 30, 2020.

Out-License Agreements

CANbridge

In March 2016, the Company entered into a collaboration and license agreement (the "CANbridge Agreement") with CANbridge Life Sciences, Ltd. ("CANbridge"). Under the terms of the CANbridge Agreement, the Company granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, the Company's proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in all countries outside of North America (the "CANbridge Licensed Territory"). In addition, CANbridge has the right of first refusal if the Company determines to out-license any North American rights. The parties have both agreed not to develop or commercialize any ErbB3 inhibitory antibody other than AV-203 during the term of the CANbridge Agreement.

Pursuant to the CANbridge Agreement, CANbridge made an upfront payment to the Company of $1.0 million in April 2016, net of $0.1 million of foreign withholding taxes. CANbridge also reimbursed the Company for $1.0 million of certain AV-203 manufacturing costs incurred by the Company prior to entering into the CANbridge Agreement. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, one in March 2017 and one in September 2017, net of foreign withholding taxes. In December 2017, CANbridge filed an investigative new drug ("IND") application with the National Medical Products Administration (formerly, the China Food and Drug Administration) ("NMPA") for a clinical study of AV-203, which CANbridge refers to as CAN017, in esophageal squamous cell carcinoma ("ESCC"). In August 2018, CANbridge obtained regulatory approval of this IND application from the NMPA and, accordingly, the Company earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018. No milestones had been achieved by CANbridge in the three months and nine months ended September 30, 2020 and 2019, respectively.

The Company is also eligible to receive up to $40.0 million in potential additional development and regulatory milestone payments and up to $90.0 million in potential commercial milestone payments based on annual net sales of licensed products. Upon commercialization, the Company is eligible to receive a tiered royalty, with a percentage range in the low double-digits, on net sales of approved licensed products. CANbridge's obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country and ten years after the first commercial sale of such licensed product in such country.

CANbridge is obligated to use commercially reasonable efforts to develop and commercialize AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge has responsibility for all activities and costs associated with the further development, manufacture and commercialization of AV-203 in the CANbridge Licensed Territory, including the clinical development of AV-203 through phase 2 proof-of-concept in ESCC or another agreed upon indication, after which the Company may elect to contribute to certain worldwide development efforts.

A percentage of any milestone and royalty payments received by the Company pursuant to the CANbridge Agreement, excluding upfront and reimbursement payments, are due to Biogen Idec International GmbH ("Biogen") as a sublicensing fee under the option and license agreement between the Company and Biogen dated March 18, 2009, as amended. The $2.0 million development and regulatory milestone the Company earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018.

Accounting Analysis Under ASC 606

The Company evaluated the CANbridge Agreement under ASC 606 and determined the CANbridge Agreement contained a single performance obligation related to the exclusive license to develop and commercialize AV-203 that was satisfied at the inception of the arrangement. The Company determined that the $1.0 million in upfront consideration received upon the execution of the CANbridge Agreement in March 2016 and the $1.0 million reimbursement received in the year ended December 31, 2017 for certain manufacturing costs incurred by the Company prior to the effective date constituted the amount of the consideration to be included in the transaction price upon the adoption of ASC 606 on January 1, 2018 and attributed these amounts to the Company's single performance obligation.

Because the Company satisfied the single performance obligation at the inception of the contract and had no remaining performance obligations, each of these amounts were recognized upon receipt. Upon adoption of ASC 606 on January 1, 2018, none of the development and regulatory milestones were included in the transaction price, as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) regulatory approvals are outside of the control of CANbridge, (ii) certain development and regulatory milestones are contingent upon the success of future clinical trials, if any, which is out of the control of CANbridge, and (iii) efforts by CANbridge. Any consideration related to development and regulatory milestones will be recognized when the corresponding milestones are no longer constrained as the Company does not have any ongoing performance obligations. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to CANbridge and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur. The Company will re-evaluate the transaction price, including its estimated variable consideration for milestones included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

In the third quarter of 2018, the Company increased the transaction price to $4.0 million to include the $2.0 million development and regulatory milestone that was earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC. Accordingly, the Company recognized the full $2.0 million amount as collaboration and licensing revenue in the year ended December 31, 2018, as the Company did not have any ongoing performance obligations under the CANbridge Agreement.

EUSA

In December 2015, the Company entered into the EUSA Agreement, under which the Company granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa and Australasia (collectively, the "EUSA Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

EUSA made research and development reimbursement payments to the Company of $2.5 million upon the execution of the EUSA Agreement during the year ended December 31, 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the European Commission in August 2017 for tivozanib (FOTIVDA) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the phase 2 clinical trial of tivozanib in combination with Opdivo® (nivolumab), a PD-1 inhibitor, in the first-line and the second-line treatment of RCC (the "TiNivo trial"). As a result of exercising its opt-in right, EUSA made an additional research and development reimbursement payment to the Company of $2.0 million. This $2.0 million payment was received in October 2017, in advance of the completion of the TiNivo trial, and represents EUSA's approximate 50% share of the total estimated costs of the TiNivo trial. The Company is also eligible to receive an additional research and development reimbursement payment from EUSA of 50% of the total costs for the Company's phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®), in 350 subjects as a third- and fourth-line treatment for RCC, including subjects with prior checkpoint inhibitor therapy (the"TIVO-3 trial"), up to $20.0 million, if EUSA elects to opt-in to that study.

The Company is entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy, Spain and the United Kingdom (collectively, the "EU5"). The Company is also entitled to receive an additional $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the EU, as mutually agreed by the parties, of which approvals have been obtained in New Zealand in July 2019 and in South Africa in October 2020. In February 2018, November 2018 and February 2019, EUSA obtained reimbursement approval from the National Institute for Health and Care Excellence ("NICE") in the United Kingdom, the German Federal Association of the Statutory Health Insurances ("GKV-SV") in Germany and the Ministry of Health, Consumer Affairs and Social Welfare ("MSCBS") in Spain, respectively, for the first-line treatment of RCC. Accordingly, the Company earned a $2.0 million milestone payment with respect to reimbursement approval in the United Kingdom that was received in March 2018, a $2.0 million milestone payment with respect to reimbursement approval in Germany that was received in December 2018 and a $2.0 million milestone payment with respect to reimbursement approval in Spain that was received in May 2019. The Company is also eligible to receive a payment of $2.0 million per indication in connection with a filing by EUSA with the EMA for marketing approval, if any, for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. The Company is also eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in the EUSA Licensed Territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. No milestone payments nor research and development reimbursement payments were earned in the three months and nine months ended September 30, 2020.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KKC, subject to certain limitations. The Company, however, would owe KKC 30% of other, non-research and development payments it may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in the EU5, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties, as set forth above. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approval for FOTIVDA from the NICE in the United Kingdom, the GKV-SV in Germany and the MSCBS in Spain, respectively, for the first-line treatment of RCC were subject to the 30% KKC sublicense fee, or $0.6 million, each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout the EUSA Licensed Territories in RCC. EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the EUSA Licensed Territories.

Accounting Analysis Under ASC 606

Pursuant to ASC 606, the Company identified the following promised goods and services at the inception of the EUSA Agreement: (i) the Company's grant of an exclusive license to develop and commercialize tivozanib in the EUSA Licensed Territories, including the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of tivozanib; (ii) the Company's obligation to cooperate with EUSA and support its efforts to file for marketing approval in the EUSA Licensed Territories and in its commercialization efforts; (iii) the Company's obligation to provide access to certain regulatory information resulting from the Company's ongoing development activities outside of the EUSA Licensed Territories; and (iv) the Company's participation in a joint steering committee. The Company determined that the license to develop and commercialize tivozanib in the EUSA Licensed Territories was not distinct from the other promised goods and services and has accordingly accounted for these items as a single performance obligation. In reaching this conclusion, the Company concluded the remaining promises were essential to EUSA's use of the license.

The Company concluded at contract inception that EUSA's opt-in rights with respect to the TiNivo trial and the TIVO-3 trial did not represent material rights because at contract inception the Company had not yet initiated either trial and the option price (representing approximately 50% of the costs of the respective trial) was proportional to the value attributed to the EUSA Licensed Territories relative to the territorial rights retained by the Company. Accordingly, the Company accounts for each opt-in as a separate arrangement when such opt-ins occur.

The Company evaluated the promised goods and services at the inception of the EUSA Agreement under ASC 606. Based on this evaluation, the Company determined that $6.5 million in research and development payments by EUSA, including the $2.5 million upfront consideration received upon the execution of the EUSA Agreement in December 2015 and the $4.0 million payment upon the receipt of marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC in August 2017, constituted the amount of the consideration that was included in the transaction price upon the adoption of ASC 606 on January 1, 2018 and attributed this amount to the Company's single performance obligation. Upon adoption of ASC 606 on January 1, 2018, none of the remaining regulatory-related milestones were included in the transaction price as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) the remaining reimbursement and marketing approvals in RCC are outside of the control of EUSA and vary on a country-by-country basis, (ii) milestones related to the submission filings for EMA approval of tivozanib in up to three additional indications are contingent upon the success of future clinical trials in additional indications, if any, and are outside of the control of EUSA, (iii) milestones related to the marketing approval by the EMA for tivozanib in up to three additional indications are contingent upon the success of the corresponding future clinical trials, if any, and are outside of the control of EUSA, and (iv) efforts by EUSA. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to EUSA and therefore are recognized at the later of when the performance obligation is satisfied (or partially satisfied) or the related sales occur. The Company will re-evaluate the transaction price, including its estimated variable consideration for milestones included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Under ASC 606, the upfront consideration and regulatory milestones included in the transaction price are being recognized as collaboration and licensing revenue over the Company's performance period from contract execution in December 2015 through the remaining patent life of tivozanib in April 2022. Under ASC 606, upon the achievement of a regulatory milestone, the amount that represents the cumulative catch-up for the period from contract execution in December 2015 through the date of the milestone achievement is recognized as collaboration and licensing revenue, with the balance classified as deferred revenue and recognized as collaboration and licensing revenue over the remainder of the performance period, currently estimated through April 2022.

In November 2017, the Company began earning sales royalties upon EUSA's commencement of the first commercial launch of tivozanib (FOTIVDA) with the initiation of product sales in Germany. EUSA has received reimbursement approval for and commercially launched FOTIVDA in Germany, the United Kingdom, and Spain as well as in some additional non-EU5 countries. EUSA is working to secure reimbursement approval in Italy and France and commercially launch FOTIVDA in additional European countries. The Company recognized royalty revenue of approximately $0.3 million and $0.2 million in the three months ended September 30, 2020 and 2019, respectively, and approximately $0.9 million and $0.6 million in the nine months ended September 30, 2020 and 2019, respectively.

In the first quarter of 2018, the Company increased the transaction price to $8.5 million to include the $2.0 million milestone for reimbursement approval from the NICE in the United Kingdom in first-line RCC that was achieved in February 2018. Accordingly, the Company recognized approximately $0.7 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in February 2018, with the approximate $1.3 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

In the fourth quarter of 2018, the Company increased the transaction price to $10.5 million to include the $2.0 million milestone for reimbursement approval from the GKV-SV in Germany in first-line RCC that was achieved in November 2018. Accordingly, the Company recognized approximately $0.9 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in November 2018, with the approximate $1.1 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

In the first quarter of 2019, the Company increased the transaction price to $12.5 million to include the $2.0 million milestone for reimbursement approval from the MSCBS in Spain in first-line RCC that was achieved in February 2019. Accordingly, the Company recognized approximately $1.0 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in February 2019, with the approximate $1.0 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

The Company recognized total revenues under the EUSA Agreement of approximately $0.8 million and $0.7 million in the three months ended September 30, 2020 and 2019, respectively, and approximately $2.3 million and $3.0 million in the nine months ended September 30, 2020 and 2019, respectively. As of September 30, 2020, there was approximately $3.0 million in total deferred revenue that is expected to continue to be recognized as collaboration and licensing revenue, in the approximate amount of $0.5 million per quarter, over the duration of the Company's performance period through April 2022.

The following table summarizes the revenues earned in connection with the EUSA Agreement under ASC 606 for the three months ended September 30, 2020 and 2019 (in thousands):

Revenue Type	Date Achieved	Three Months Ended September 30, 2020	Three Months Ended September 30, 2019
Collaboration and Licensing Revenue:			
Amounts in contract liabilities at the beginning of the period:			
Upfront payment	December 2015	$ 98	$ 99
R&D payment - EMA approval in RCC	August 2017	158	158
Milestone - UK reimbursement approval	February 2018	79	79
Milestone - German reimbursement approval	November 2018	79	79
Milestone - Spanish reimbursement approval	February 2019	79	79
		$ 493	$ 494
Partnership Royalties		307	223
Total		$ 800	$ 717

The following table summarizes the revenues earned in connection with the EUSA Agreement under ASC 606 for the nine months ended September 30, 2020 and 2019 (in thousands):

Revenue Type	Date Achieved	Nine Months Ended September 30, 2020	Nine Months Ended September 30, 2019
Collaboration and Licensing Revenue:			
Amounts in contract liabilities at the beginning of the period:			
Upfront payment	December 2015	$ 296	$ 296
R&D payment - EMA approval in RCC	August 2017	473	474
Milestone - UK reimbursement approval	February 2018	237	237
Milestone - German reimbursement approval	November 2018	237	237
Milestone - Spanish reimbursement approval	February 2019	237	1,197
		$ 1,480	$ 2,441
Partnership Royalties		853	590
Total		$ 2,333	$ 3,031

The following table summarizes changes in the Company's accounts receivable and contract liabilities (deferred revenue) in connection with the EUSA Agreement for the nine months ended September 30, 2020 (in thousands):

Contract Assets	Beginning Balance January 1, 2020	Additions	Deductions	Ending Balance September 30, 2020
Accounts Receivable	$ 270	$ 853	$ (816)	$ 307

Contract Liabilities	Transaction Price	Date Achieved	Date Paid	Deferred Revenue: Beginning Balance January 1, 2020	Additions	Deductions	Ending Balance September 30, 2020
Amounts in contract liabilities at the beginning of the period:							
Upfront payment	$ 2,500	December 2015	December 2015	$ 907	$ —	$ (296)	$ 611
R&D payment - EMA approval in RCC	4,000	August 2017	September 2017	1,448	—	(473)	975
Milestone - UK reimbursement approval	2,000	February 2018	March 2018	724	—	(237)	487
Milestone - German reimbursement approval	2,000	November 2018	December 2018	723	—	(237)	486
Milestone - Spanish reimbursement approval	2,000	February 2019	May 2019	724	—	(237)	487
Total	$ 12,500			$ 4,526	$ -	$ (1,480)	$ 3,046

Opt-In to the TiNivo Trial

In September 2017, EUSA elected to opt-in to co-develop the TiNivo trial. As previously described, the Company accounts for each opt-in as a separate arrangement. As a result of EUSA's exercise of its opt-in right, it became an active participant in the ongoing conduct of the TiNivo trial and is able to utilize the resulting data from the TiNivo trial for regulatory and commercial purposes in the EUSA Licensed Territories. Upon the exercise of its opt-in right, EUSA became responsible for funding 50% of the total estimated costs of the TiNivo trial, up to $2.0 million. The Company is accounting for the joint development activities relative to the TiNivo trial as a joint risk-sharing collaboration in accordance with ASC 808 because EUSA is an active participant in the ongoing TiNivo trial and is exposed to significant risk and rewards in connection with the activity. Payments from EUSA with respect to its share of TiNivo trial development costs incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities that is not representative of a vendor-customer relationship.

The Company recognized reductions in research and development expenses of approximately $5 thousand and $0 in the three months ended September 30, 2020 and 2019, respectively, and approximately $0.1 million and $0.2 million in the nine months ended September 30, 2020 and 2019, respectively. As of September 30, 2020, the Company had recognized approximately $1.9 million in cumulative total reductions in research and development expenses related to EUSA's approximate 50% share of the cumulative study-to-date costs. EUSA paid the $2.0 million maximum amount of cost sharing per the EUSA Agreement in advance of the completion of the trial. The remaining $0.1 million in prepaid cost sharing was classified as deferred research and development reimbursements as of September 30, 2020 and will continue to be recognized as a reduction in research and development expenses as the related TiNivo trial costs are incurred over the duration of the trial.

Novartis

In August 2015, the Company entered into a license agreement (the "Novartis Agreement") with Novartis International Pharmaceutical, Ltd. ("Novartis"), under which the Company granted Novartis the exclusive right to develop and commercialize AV-380 and the Company's related antibodies worldwide. On June 29, 2018, Novartis notified the Company that it would be terminating the Novartis Agreement without cause, following a change in strategic direction at Novartis. Effective August 28, 2018 the Company regained the rights to AV-380, and on December 19, 2018, the Company entered into a new agreement with Novartis (the "AV-380 Transfer Agreement") to further establish and clarify the terms on which Novartis would return the AV-380 program to the Company and to support the Company's continuing development of the AV-380 program. Pursuant to the AV-380 Transfer Agreement, Novartis made a one-time payment to the Company of $2.3 million in January 2019, which the Company used to cover the $2.3 million time-based milestone obligation due to St. Vincent's Hospital Sydney Limited ("St. Vincent's") in January 2019 under its license agreement as further described below under the heading "—In-License Agreements – St. Vincent's."

In connection with the AV-380 Transfer Agreement, the $2.3 million payment due from Novartis was not considered a revenue transaction due to the effective termination of the Novartis Agreement on August 28, 2018 and was instead considered other income. The Company evaluated the return of the AV-380 drug supply and determined that the inventory was not capitalizable as future economic benefit was not probable due to the AV-380 drug candidate being in the pre-clinical development stage.

Biodesix

In April 2014, the Company entered into a worldwide co-development and collaboration agreement (the "Biodesix Agreement") with Biodesix, Inc. ("Biodesix") to develop and commercialize ficlatuzumab, the Company's HGF inhibitory antibody. In September 2020, the Company regained full global rights to ficlatuzumab, effective December 2, 2020, when Biodesix exercised its "Opt-Out" rights (as defined below) under the Biodesix Agreement.

Under the Biodesix Agreement, the Company granted Biodesix perpetual, non-exclusive rights to certain intellectual property, including all clinical and biomarker data related to ficlatuzumab, to develop and commercialize VeriStrat®, Biodesix's proprietary companion diagnostic test. Biodesix granted the Company perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to VeriStrat, with respect to the development and commercialization of ficlatuzumab. Each license included the right to sublicense, subject to certain exceptions. The Company was designated to lead the clinical development of ficlatuzumab following approval of a development plan by a joint steering committee. The Company and Biodesix are currently funding an investigator-sponsored clinical trial for ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC. The Biodesix Agreement generally provided for each party to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab and to share equally in any future revenue from development or commercialization.

Under the Biodesix Agreement, prior to the first commercial sale of ficlatuzumab, each party had the right to elect to discontinue its funding obligation for further development or commercialization efforts with respect to ficlatuzumab in exchange for reduced economics in the program, which is referred to as an “Opt-Out.” Pursuant to the terms of the Biodesix Agreement, as a result of Biodesix’s election to Opt-Out, Biodesix will (i) continue to be responsible for reimbursement of development costs with respect to the ongoing open label Phase 2 investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC, (ii) cease to be entitled to 50% sharing of profits resulting from commercialization of ficlatuzumab, (iii) be entitled to a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses) less approximately $2.5 million Biodesix would be required to pay to the Company pursuant to the October 2016 amendment to the Biodesix Agreement and (iv) remain responsible for development obligations under the Biodesix Agreement with respect to VeriStrat. Biodesix and the Company also remain obligated to negotiate a commercialization agreement to delineate their rights and obligations in the event of any commercialization of VeriStrat with ficlatuzumab. As a result of Biodesix’s decision to Opt-Out, the Company now has sole decision-making authority with respect to further development and commercialization of ficlatuzumab. The Biodesix Agreement will remain in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

The Company is accounting for the joint development activities under the Biodesix Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and Biodesix have been active participants in the ongoing development of ficlatuzumab via their participation on a joint steering committee that oversaw the development plans for ficlatuzumab and have been exposed to significant risk and rewards in connection with their activity based on their obligations to share in the costs, as defined above. Payments from Biodesix with respect to its share of ficlatuzumab development costs incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities that is not representative of a vendor-customer relationship.

The Company records reimbursements from Biodesix for expenses related to these trials and drug manufacturing as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the Biodesix Agreement, the Company reduced research and development expenses by approximately $0.1 million and $0.2 million in the three months ended September 30, 2020 and 2019, respectively, and by approximately $0.8 million and $0.4 million in the nine months ended September 30, 2020 and 2019, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $0.1 million as of September 30, 2020.

Biogen Idec International GmbH

In March 2009, the Company entered into an exclusive option and license agreement with Biogen regarding the development and commercialization of the Company’s discovery-stage ErbB3-targeted antibodies, including AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of North America (the “Biogen Agreement”). Under the Biogen Agreement, the Company was responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, would generate data sufficient to support advancement to a phase 3 clinical trial.

In March 2014, the Company and Biogen amended the Biogen Agreement (the “Biogen Amendment”). Pursuant to the Biogen Amendment, Biogen agreed to the termination of its rights and obligations under the Biogen Agreement, including Biogen’s option to (i) obtain a co-exclusive (with the Company) worldwide license to develop and manufacture ErbB3 targeted antibodies and (ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. As a result, the Company has worldwide rights to AV-203. Pursuant to the Biogen Amendment, the Company was obligated to use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The Company is also obligated to pay Biogen a percentage of milestone payments received by the Company from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, if any, up to a cumulative maximum amount of $50.0 million.

In March 2016, the Company entered into a collaboration and license agreement for AV-203 with CANbridge, which satisfied its obligation to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The $2.0 million development and regulatory milestone the Company earned in August 2018 in connection with CANbridge’s regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018. Refer to “—*CANbridge*” within this Note 4 for a further description of that arrangement.

In-License Agreements

St. Vincent's

In July 2012, the Company entered into a license agreement with St. Vincent's, under which the Company obtained an exclusive, worldwide sublicensable right to research, develop, manufacture and commercialize products for human therapeutic, preventative and palliative applications that benefit from inhibition or decreased expression or activity of GDF15, which is also referred to as MIC-1 (the "St. Vincent's Agreement"). Under the St. Vincent's Agreement, St. Vincent's also granted the Company non-exclusive rights for certain related diagnostic products and research tools.

In order to sublicense certain necessary intellectual property rights to Novartis in August 2015, the Company amended and restated the St. Vincent's Agreement and made an additional upfront payment to St. Vincent's of $1.5 million. As of September 30, 2020, the Company is required to make future milestone payments, up to an aggregate total of $14.4 million, upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third indications, for licensed therapeutic products, some of which payments may be increased by a mid to high double-digit percentage rate for milestones payments made after the Company grants any sublicense, depending on the sublicensed territory. In February 2017, Novartis agreed to pay $1.8 million out of its then future payment obligations to the Company under the Novartis Agreement. These funds were used to satisfy a $1.8 million time-based milestone obligation that the Company owed to St. Vincent's in March 2017. As further described above under the heading "—*Out-License Agreements Novartis*", the Company used the $2.3 million payment received from Novartis in January 2019, pursuant to the AV-380 Transfer Agreement, to cover a $2.3 million time-based milestone obligation that became due to St. Vincent's in January 2019. The Company will also be required to pay St. Vincent's tiered royalty payments equal to a low-single-digit percentage of any net sales it or its sublicensees make from licensed therapeutic products. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year.

Kyowa Kirin Co. (KKC)

In December 2006, the Company entered into the KKC Agreement with KKC, under which it obtained an exclusive, sublicensable license to develop, manufacture and commercialize tivozanib in all territories in the world except for Asia and the Middle East, where KKC retained the rights to tivozanib. Under the KKC Agreement, the Company obtained exclusive rights to tivozanib in its territory under certain KKC patents, patent applications and know-how for the diagnosis, prevention and treatment of all human diseases and conditions (the "Field"). On August 1, 2019, the Company entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in the Company's territory, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. The Company has upfront, milestone and royalty payment obligations to KKC under the KKC Agreement related to the amended Field for oncology development by the Company, and following the amendment, KKC also has upfront, milestone and royalty payment obligations to the Company related to non-oncology development by KKC in the Company's territory. Pursuant to the amendment to the KKC Agreement, KKC was required to make a non-refundable upfront payment to the Company in the amount of $25.0 million that was received in September 2019 and KKC waived a one-time milestone payment of $18.0 million otherwise payable by the Company upon obtaining marketing approval for tivozanib in the U.S.

Upon entering into the KKC Agreement, the Company made an upfront payment in the amount of $5.0 million. In March 2010, the Company made a milestone payment to KKC in the amount of $10.0 million in connection with the dosing of the first patient in the Company's TIVO-1 trial. In December 2012, the Company made a $12.0 million milestone payment to KKC in connection with the acceptance by the FDA of the Company's 2012 NDA filing for tivozanib. Each milestone under the KKC Agreement is a one-time only payment obligation, accordingly, the Company did not owe KKC another milestone payment in connection with the dosing of the first patient in the Company's TIVO-3 trial, and would not owe a milestone payment to KKC when the Company filed its then anticipated NDA with the FDA, which was subsequently filed on March 31, 2020. The Company has no remaining development and commercialization milestone payments due to KKC under the KKC Agreement.

If the Company sublicenses any of its rights to tivozanib to a third party, as it has done with EUSA, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under the KKC Agreement relating to rights the Company retains. The Company is required to pay KKC a fixed 30% of amounts the Company receives from its sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts the Company receives in respect of research and development reimbursement payments or equity investments, subject to certain limitations. Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million payment in September 2017 upon the receipt of marketing authorization from the European Commission for tivozanib (FOTIVDA) and the $2.0 million payment upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial, were not subject to sublicense revenue payments to KKC. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of 50% of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KKC, subject to certain limitations. The Company would, however, owe KKC 30% of other, non-research and development payments the Company may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in up to five specified EU countries, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approvals for FOTIVDA as a first-line treatment for RCC in the United Kingdom, Germany and Spain, respectively, were subject to the 30% KKC sublicense fee, or $0.6 million each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its North American territory, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. The Company's royalty payment obligations in a particular country in its territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country.

In addition to the non-refundable upfront payment to the Company pursuant to the amendment to the KKC Agreement in the amount of $25.0 million, KKC is also required to make milestone payments to the Company of up to an aggregate of $390.7 million upon the successful achievement of certain development and sales milestones of tivozanib in non-oncology indications. On August 2, 2020, KKC's IND application for a non-oncology formulation of tivozanib was accepted by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company earned a $2.8 million development milestone payment upon acceptance of the IND pursuant to the KKC Agreement that was received in August 2020. In addition, KKC is required to make tiered royalty payments to the Company on net sales of tivozanib in non-oncology indications in the Company's territory, which range from high single digit to low double digits as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales, subject to certain adjustments. KKC's royalty payment obligations in a particular country in the Company's territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of the expiration date of the last valid claim of a patent application or patent owned by KKC covering tivozanib or 10 years after the date of first commercial sale of tivozanib in non-oncology indications in that country.

If KKC sublicenses any of its rights to tivozanib to a third party, KKC is required to pay the Company a percentage of amounts received from the respective sublicensees related to the Company's territory, including upfront license fees, milestone payments and royalties, but excluding amounts received in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

The Company and KKC each have access to and can benefit from the other party's clinical data and regulatory filings with respect to tivozanib and biomarkers identified in the conduct of activities under the KKC Agreement, as related to the amended Field for oncology development. Under the KKC Agreement, the Company is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in its territory.

The KKC Agreement will remain in effect until the expiration of all of the Company's royalty and sublicense revenue obligations, determined on a product-by-product and country-by-country basis, unless terminated earlier. If the Company fails to meet its obligations under the KKC Agreement and is unable to cure such failure within specified time periods, KKC can terminate the KKC Agreement, resulting in a loss of our rights to tivozanib and an obligation to assign or license to KKC any intellectual property or other rights the Company may have in tivozanib, including its regulatory filings, regulatory approvals, patents and trademarks for tivozanib.

Accounting Analysis Under the August 1, 2019 Amendment to the KKC Agreement

Following the repurchase of non-oncology rights by KKC, the amended KKC Agreement is accounted for as two distinct agreements: (i) the KKC Agreement by which the Company has upfront, milestone and royalty payment obligations to KKC related to the Company's oncology development of tivozanib in the amended Field for the Company's territory that continues to be accounted for under ASC 730, *Research and Development,* and (ii) the amended KKC Agreement by which KKC has upfront, milestone and royalty payment obligations to the Company related to its non-oncology development of tivozanib for the Company's territory that will be accounted for under ASC 606.

The Company evaluated the amendment to the KKC Agreement under ASC 606 and determined that KKC met the definition of a customer as the Company considers the licensing or sale of intellectual property rights to be an output of the Company's ordinary activities and is central to the operations of the Company. The Company determined that the amendment to the KKC Agreement contained a single performance obligation related to the Company's transfer of rights to non-oncology intellectual property and know-how to KKC, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. In addition, the Company determined that the $25.0 million non-refundable upfront payment received from KKC in September 2019 constituted the amount of the consideration to be included in the transaction price and attributed this amount to the Company's single performance obligation. The Company satisfied this performance obligation during the third quarter of 2019. Accordingly, the Company recognized the $25.0 million in consideration as revenue in the third quarter of 2019. The Company concluded the performance obligation was satisfied at a point in time because any know-how or clinical data generated from the Company's ongoing oncology development of tivozanib would not benefit KKC's non-oncology development of tivozanib.

In the third quarter of 2020, the Company increased the transaction price to $27.8 million to include the $2.8 million development milestone that was earned in August 2020 upon the acceptance of KKC's IND application for a non-oncology formulation of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company recognized the $2.8 million in consideration as revenue in the third quarter of 2020 as the Company did not have any ongoing performance obligations under the amendment to the KKC Agreement.

None of KKC's development and regulatory milestones to the Company related to its non-oncology development of tivozanib for the Company's territory were included in the transaction price, as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) regulatory approvals are outside of the control of KKC, (ii) certain development and regulatory milestones are contingent upon the success of future clinical trials, if any, which is out of the control of KKC, and (iii) efforts by KKC. Any consideration related to development and regulatory milestones owed by KKC to the Company will be recognized when the corresponding milestones are no longer constrained as the Company does not have any ongoing performance obligations. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the intellectual property transferred to KKC and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur.

(5) Other Accrued Liabilities

Other accrued expenses consisted of the following (in thousands):

	September 30, 2020	December 31, 2019
Professional fees	$ 832	$ 806
Compensation and benefits	2,215	1,284
Other	364	246
Total	$ 3,411	$ 2,336

(6) Hercules Loan Facility

On May 28, 2010, the Company entered into a loan and security agreement with Hercules Capital Inc. and certain of its affiliates (the "First Loan Agreement"). The First Loan Agreement was subsequently amended in March 2012, September 2014 and May 2016 (the "2016 Amendment"). Amounts borrowed under the amendment in 2012 were repaid in full in 2015.

In December 2017, the Company entered into an amended and restated loan and security agreement (the "2017 Loan Agreement") to refinance the Company's prior loan facility with Hercules and to retire the $20.0 million in secured debt then-outstanding under the First Loan Agreement. Per the terms of the 2017 Loan Agreement, the $20.0 million loan facility had a 42-month maturity from closing, no financial covenants, a lower interest rate and an interest-only period of no less than 12 months, which could be extended up to a maximum of 24 months, assuming the achievement of specified milestones relating to the development of tivozanib.

Per the 2017 Loan Agreement, the loan maturity date was revised from December 2019 to July 2021. The Company was not required to make principal payments until February 1, 2019, at which time the Company would have been required to make 29 equal monthly payments of principal and interest, in the approximate amount of $0.8 million, through July 2021. An additional end-of-term payment of approximately $0.8 million is due on July 1, 2021. The financial covenant per the 2016 Amendment to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of the Company's TIVO-3 trial with results that are satisfactory to Hercules was removed. Per the 2017 Loan Agreement, the interest rate decreased from 11.9% to 9.45%. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which was accounted for as a loan discount. The 2017 Loan Agreement was accounted for as a loan modification in accordance with ASC 470-50, *Modifications and extinguishments* ("ASC 470-50").

The Company must make interest payments on the principal balance of the loan each month it remains outstanding. Per annum interest was payable on the loan balance at the greater of 9.45% and an amount equal to 9.45% plus the prime rate minus 4.75%, as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. In 2018, the interest rate increased to 9.70%, 9.95% and 10.20% in June 2018, September 2018 and December 2018, respectively, due to corresponding increases in the prime rate. In 2019, the interest rate decreased to 9.95%, 9.70% and 9.45% in August 2019, September 2019 and October 2019, respectively, due to corresponding decreases in the prime rate. The interest rate as of August 1, 2020 was 9.45%.

The interest-only period could be extended by two 6-month deferrals of principal payments upon the achievement of specified milestones relating to the development of tivozanib, subject to confirmation by Hercules at its reasonable discretion.

In November 2018, Hercules granted the first 6-month extension of the interest-only period. Accordingly, this resulted in the deferment of principal payments until August 1, 2019, at which time the Company resumed making 24 equal monthly payments of principal and interest, in the approximate amount of $0.9 million through July 2021. The outstanding principal balance as of August 1, 2020 was approximately $9.7 million.

On August 7, 2020, the Company entered into a first amendment to the 2017 Loan Agreement (the "2020 Loan Amendment") to provide the Company, subject to certain terms and conditions, with an additional term loan in an aggregate principal amount of up to $35.0 million (the "2020 Loan Facility") in up to four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement, and for general working capital purposes.

The Company received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, of which approximately $9.7 million was used to retire the outstanding balance under the 2017 Loan Agreement and of which approximately $5.3 million is new loan funding.

The remainder of the loan amount will be available to the Company, at its option, subject to certain terms and conditions, including upon the achievement of the following milestones: (i) the second tranche of $10.0 million would be available through June 30, 2021 assuming FDA approval of FOTIVDA ("Performance Milestone I"), (ii) the third tranche of $5.0 million ("Tranche Three") would be available from July 1, 2021 through January 31, 2022 assuming the Company achieves $20.0 million in net product revenues from sales of FOTIVDA, if approved by the FDA, by no later than December 31, 2021 ("Performance Milestone II"), and (iii) the fourth tranche of $5.0 million would be available through June 30, 2022 contingent upon the achievement of both Performance Milestone I and Performance Milestone II, and subject to the consent of Hercules.

The 2020 Loan Facility also amends the 2017 Loan Agreement by: (i) extending maturity until September 1, 2023, which is extendable to September 1, 2024 at the Company's option assuming the Tranche Three funding has occurred, (ii) providing for an interest-only period through September 30, 2021, which is extendable through September 30, 2022, if at all, upon the achievement of Performance Milestone I and further extendable through March 31, 2023 after the Tranche Three funding has occurred, if at all, and

(iii) revising the per annum interest rate to the greater of (x) 9.65% and (y) an amount equal to 9.65% plus the prime rate as reported in the Wall Street Journal minus 3.25% as determined daily, provided however, that the per annum interest rate shall not exceed 15%. Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of September 30, 2020 was 9.65%.

Per the terms of the 2020 Loan Facility, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. The Company may prepay all of the outstanding principal and accrued interest under the 2020 Loan Facility, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. The Company is obligated to make an end-of-term payment of 6.95% of the aggregate amount of loan funding received under the 2020 Loan Facility on the earlier of the maturity of the loan or the date on which the Company prepays any outstanding loan balance. The approximate $0.8 million end-of-term payment under the 2017 Loan Agreement continues to be due on July 1, 2021. In connection with the 2020 Loan Amendment, the Company incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The unamortized discount to be recognized over the remainder of the loan period was approximately $1.4 million and $0.4 million as of September 30, 2020 and December 31, 2019, respectively.

The 2020 Loan Facility includes various financial and operating covenants, including that the Company maintain an unrestricted cash position of at least $10.0 million through the date the Third Tranche funding is received and at least $5.0 million thereafter through the maturity of the loan. The Company is also required to achieve greater than or equal to 75% of its forecasted net product revenues from its sales of FOTIVDA over a 6-month trailing period, as defined and measured on a monthly basis, effective upon the Third Tranche funding and continuing through the maturity of the loan. The net product revenue covenant will not apply at any time the Third Tranche funding has not been provided nor such advance has been prepaid in full.

The 2020 Loan Facility is secured by substantially all of the Company's assets, excluding intellectual property. The 2020 Loan Facility provides that certain events shall constitute a default by the Company, including failure by the Company to pay amounts under the 2020 Loan Amendment when due; breach or default in the performance of any covenant under the 2020 Loan Amendment by the Company, subject to certain cure periods; insolvency of the Company and certain other bankruptcy proceedings involving the Company; default by the Company of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon the business of the Company. As of September 30, 2020, the Company was in compliance with all loan covenants, Hercules has not asserted any events of default and the Company does not believe that there has been a material adverse change as defined in the 2020 Loan Amendment.

The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal as a long-term liability based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of September 30, 2020 are as follows (amounts in thousands):

Year Ending December 31:		
2020 (remaining 3 months)		366
2021		3,961
2022		8,277
2023		7,272
		19,876
Less amount representing interest		(3,043)
Less unamortized discount		(1,383)
Less deferred charges		(1,833)
Less loans payable current, net of discount		—
Loans payable, net of current portion and discount	$	13,617

(7) Common Stock

As of September 30, 2020, the Company had 50,000,000 authorized shares of common stock, $0.001 par value, of which 25,808,315 shares were issued and outstanding.

Reverse Stock Split – February 2020

On February 13, 2020, the holders of a majority of the Company's outstanding shares of common stock approved the reverse stock split and gave the Company's board of directors discretionary authority to select a ratio for the split ranging from 1-for-5 to 1-for-15. The Company's board of directors approved the reverse stock split at a ratio of 1-for-10 on February 13, 2020. On February 19, 2020, the Company effected a reverse stock split of its outstanding shares of common stock at a ratio of one-for-ten pursuant to a Certificate of Amendment to its Certificate of Incorporation filed with the Secretary of State of the State of Delaware. The reverse stock split was reflected on Nasdaq beginning with the opening of trading on February 20, 2020. The primary purpose of the reverse stock split was to enable the Company to regain compliance with the $1.00 minimum bid price requirement for continued listing on Nasdaq.

The reverse stock split affected all issued and outstanding shares of the Company's common stock, as well as the number of authorized shares of the Company's common stock and the number of shares of common stock available for issuance under the Company's equity incentive plans. The reverse stock split reduced the number of shares of the Company's issued and outstanding common stock from approximately 160.8 million to approximately 16.1 million. In addition, the reverse stock split effected a reduction in the number of shares of the Company's common stock issuable upon the exercise of stock options and warrants outstanding immediately prior to the reverse stock split, with a proportional increase in the respective exercise prices. The reverse stock split proportionately reduced the number of authorized shares of the Company's common stock from 500.0 million shares to 50.0 million shares. The reverse stock split did not change the par value of the Company's common stock or the authorized number of shares of the Company's preferred stock. All share and per share amounts give effect to the reverse stock split on a retroactive basis.

Public Offering – June 2020

On June 19, 2020, the Company completed an underwritten public offering of 9,725,000 shares of its common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders beneficially holding more than 5% of the Company's voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders, purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

Public Offering – April 2019

In April 2019, the Company completed an underwritten public offering of 2,173,913 shares of its common stock and warrants to purchase an aggregate of 2,500,000 shares of its common stock ("the Offering Warrants"), including warrants to purchase an aggregate of 326,086 shares of its common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and will expire two years from the date of issuance upon their scheduled expiration on April 8, 2021. Any Offering Warrants that have not been exercised for cash prior to their expiration shall be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and are separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately $22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. As of September 30, 2020, Offering Warrants to purchase 2,500,000 shares of the Company's common stock were outstanding. The Company determined the shares of common stock and the Offering Warrants represented freestanding financial instruments. In addition, the Company conducted an assessment of the classification of the Offering Warrants and, based on their terms, concluded the Offering Warrants are equity-classified. Accordingly, the net offering proceeds of $22.8 million have been recorded within stockholders' equity (deficit).

Sales Agreement with SVB Leerink

In February 2018, the Company entered into the a sales agreement (the "Leerink Sales Agreement,") with SVB Leerink LLC ("SVB Leerink") pursuant to which the Company may issue and sell shares of its common stock from time to time up to an aggregate amount of $50.0 million, at its option, through SVB Leerink as its sales agent, with any sales of common stock through SVB Leerink being made by any method that is deemed an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the "Securities Act"), or in other transactions pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. In the fourth quarter of 2018, the Company sold 470,777 shares pursuant to the Leerink Sales Agreement, resulting in approximately $10.3 million in proceeds, net of commissions. In February 2019, the Company sold 1,251,555 shares pursuant to the Leerink Sales Agreement, resulting in proceeds of approximately $7.5 million, net of commissions. As of September 30, 2020, approximately $32 million was available for issuance in connection with future stock sales pursuant to the Leerink Sales Agreement.

Settlement Warrants

On July 16, 2018, the Company issued and delivered 200,000 warrants to purchase shares of its common stock that the Company agreed to issue in connection with the settlement of the former 2013 class action lawsuit (the "Settlement Warrants"). The Settlement Warrants were exercisable for a one-year period after the date of issuance at an exercise price equal to $30.00 per share. All 200,000 Settlement Warrants expired on July 15, 2019 as none of the warrants had been exercised during the one-year exercise period.

Universal Shelf Registration Statement

On November 30, 2017, the Company filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of up to $200.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2017 Shelf"). The 2017 Shelf (File No. 333-221873) was declared effective by the SEC on December 15, 2017 and was filed to replace the Company's then existing shelf registration statement, which was terminated. As of September 30, 2020, approximately $37 million was available for issuance in connection with future stock sales under the 2017 Shelf.

Private Placement – May 2016

In May 2016, the Company entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which the Company sold 1,764,242 units, at a price of $9.65 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of the Company's common stock and a warrant to purchase one share of the Company's common stock (the "PIPE Warrants"). The PIPE Warrants have an exercise price of $10.00 per share and are exercisable for a period of five years from the date of issuance until their scheduled expiration on May 16, 2021. Certain of the Company's directors and executive officers purchased an aggregate of 54,402 units in this offering at the same price as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by the Company. As of September 30, 2020, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding.

(8) Stock-based Compensation

Stock Incentive Plan

The Company previously maintained the 2010 Stock Incentive Plan (the "2010 Plan") for employees, consultants, advisors, and directors, as amended in March 2013, June 2014 and June 2017.

In April 2019, the Company's Board of Directors adopted the 2019 Equity Incentive Plan (the "2019 Plan") and on June 12, 2019 the stockholders approved the 2019 Plan at the Annual Meeting of Stockholders. The 2019 Plan provides similar terms as the 2010 Plan, including: (i) a provision for the grant of equity awards such as stock options and restricted stock, (ii) that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the grant for participants who own less than 10% of the total combined voting power of stock of the Company and not less than 110% for participants who own more than 10% of the total combined voting power of the stock of the Company, (iii) that options and restricted stock granted under the 2019 Plan vest over periods as determined by the Board of Directors, which generally are equal to four years, and (iv) that options granted under the 2019 Plan expire over periods as determined by the Board of Directors, which generally are ten years from the date of grant. In April 2020, the Board of Directors adopted an amendment to the 2019 Plan to increase the total number of shares reserved under the Plan by 1,300,000 shares, among other things. The amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 10, 2020.

Awards may be made under the 2019 Plan for up to the sum of (i) 2,300,000 shares of common stock and (ii) such additional number of shares of common stock (up to 1,068,901 shares) as is equal to (x) the number of shares of common stock reserved for issuance under the 2010 Plan that were available for grant under the 2010 Plan immediately prior to the date the 2019 Plan was approved by the Company's stockholders and (y) the number of shares of common stock subject to awards outstanding under the 2010 Plan, which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company pursuant to a contractual repurchase right. As of September 30, 2020, there were 1,670,211 shares of common stock available for future issuance under the 2019 Plan and no shares of common stock available for future issuance under the 2010 Plan.

The following table summarizes stock option activity during the nine months ended September 30, 2020:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2020	1,168,222	$ 16.77		
Granted	603,482	$ 5.86		
Exercised	—	$ —		
Forfeited	(81,009)	$ 17.06		
Outstanding at September 30, 2020	1,690,695	$ 12.86	7.50	$ 230,000
Exercisable at September 30, 2020	860,401	$ 17.58	6.04	$ 18,000

The aggregate intrinsic value is based upon the Company's closing stock price of $5.94 on September 30, 2020.

The fair value of stock options subject only to service or performance conditions that are granted to employees is estimated on the date of grant using the Black-Scholes option-pricing model using the assumptions noted in the table below.

	Three Months Ended September 30,	
	2020	2019
Volatility factor	98.99% - 99.19%	96.30%
Expected term (in years)	6.25	6.25
Risk-free interest rates	0.31% - 0.42%	1.89%
Dividend yield	—	—

	Nine Months Ended September 30,	
	2020	2019
Volatility factor	94.37% - 102.48%	88.27% - 96.30%
Expected term (in years)	5.50 - 6.25	5.50 - 6.25
Risk-free interest rates	0.31% - 1.67%	1.89% - 2.55%
Dividend yield	—	—

The risk-free interest rate is determined based upon the United States Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the options being valued. The Company does not expect to pay dividends in the foreseeable future.

Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the nine months ended September 30, 2020 and 2019 was $4.55 and $5.80, respectively.

As of September 30, 2020, there was $5.0 million of total unrecognized stock-based compensation expense related to stock options granted to employees under the Plan. The expense is expected to be recognized over a weighted-average period of 2.75 years.

(9) Legal Proceedings

On July 24, 2020, the District Court for the District of Massachusetts dismissed a purported class action filed against the Company in 2019. This purported class action lawsuit (the "2019 Class Action") was filed against the Company and certain of its present and former officers, Michael Bailey, Matthew Dallas, and Keith Ehrlich, in the Southern District of New York for the District of New York, captioned *David Hackel v. AVEO Pharmaceuticals, Inc., et al*, No. 1:19-cv-01722-AT. On April 12, 2019, the court granted the defendants' motion to transfer the action to the District of Massachusetts (Case No. 1:19-cv-10783-JCB). On May 6, 2019, the court appointed Andrej Hornak as lead plaintiff and approved Pomerantz LLP as lead counsel and Andrews DeValerio LLP as liaison counsel. On July 24, 2019, the plaintiffs filed an amended complaint naming Michael Needle as a defendant. The amended complaint purported to be brought on behalf of shareholders who purchased the Company's common stock between May 4, 2017 through January 31, 2019. It generally alleged that the Company and its officers violated Sections 10(b) and/or 20(a) of the Securities

Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by failing to disclose and/or making allegedly false and/or misleading statements about the estimated dates by which the Company would report the topline results from the TIVO-3 trial, the preliminary overall survival results from the TIVO-3 trial, the sufficiency of the overall survival data from the TIVO-3 trial, the timing of the NDA submission, and the risk of FDA approval. The complaint sought unspecified damages, interest, attorneys' fees, and other costs. On September 27, 2019, the defendants filed a motion to dismiss the amended complaint. On July 24, 2020, the District Court granted the Company's motion to dismiss. The time for appeal expired in August 2020 without appeal.

In connection with the filing of the 2019 Class Action, two derivative lawsuits were filed on July 8, 2019 and July 10, 2019 against the Company, certain of its present and former officers and its directors in the Suffolk Superior Court, Commonwealth of Massachusetts, captioned *Stephen Favre v. Michael P. Bailey, et al*. 19-2169-BLS2 and *Jianbin Yu v. Michael P. Bailey, et al.* 19-2188-BLS2, respectively. The complaints generally allege breach of fiduciary duty, unjust enrichment, and waste of corporate assets due to the 2019 Class Action and the actions alleged therein. On July 26, 2019, the court granted the parties'joint motion to consolidate the cases and stay the consolidated matter pending the dismissal of, or filing of an answer to, the complaint in the 2019 Class Action. Given the dismissal of the 2019 Class Action in July 2020, the derivative plaintiffs have agreed to dismiss the derivative lawsuit without prejudice. The Company anticipates a stipulation will be filed with the court soon.

In June 2018, the Company settled a consolidated class action lawsuit (the "2013 Class Action"), *In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC*, that had been filed in 2013 against the Company and certain of its former officers (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer, and Ronald DePinho) in the United States District Court for the District of Massachusetts (the "District Court"). The 2013 Class Action had been dismissed without prejudice in March 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations, but which no longer named Mr. DePinho as a defendant. The Company moved to dismiss again, and the District Court ruled in the Company's favor and dismissed the second amended complaint with prejudice in November 2015. The lead plaintiffs appealed the District Court's decision and also filed a motion to vacate and reconsider the District Court's judgment. In January 2017, the District Court granted the plaintiffs' motion to vacate the dismissal and judgment. In February 2017, the plaintiffs filed a third amended complaint, on behalf of stockholders who purchased common stock between May 16, 2012 and May 1, 2013 (the "2013 Class") alleging claims similar to those alleged in the prior complaints, namely that the Company and certain of the Company's former officers and directors violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the phase 3 trial design and results for the Company's TIVO-1 clinical trial in an effort to lead investors to believe that the drug would receive approval from the FDA. In July 2017, the District Court entered an order referring the case to alternative dispute resolution. The parties mediated during the fall of 2017.

On December 26, 2017, the parties entered into a binding memorandum of understanding (the "MOU") to settle the 2013 Class Action. Under the terms of the MOU, the Company agreed to cause certain of the Company's and the individual defendants' insurance carriers to provide the 2013 Class with a cash payment of $15.0 million, which included the cash amount of any attorneys' fees or litigation expenses that the District Court may award. Additionally, the Company agreed to issue to the 2013 Class the Settlement Warrants, for the purchase of 0.2 million shares of the Company's common stock, which, subject to certain conditions, are exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price of $3.00 per share, equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU. On January 29, 2018, the parties entered into a definitive Stipulation of Settlement (the "Stipulation"), which was filed with the District Court on February 2, 2018. On February 8, 2018, the District Court issued an order preliminarily approving the terms of the Stipulation. In February 2018, the insurance carriers funded the settlement escrow account for the $15.0 million cash settlement. On May 30, 2018, the District Court held the final approval hearing and approved the settlement and the plaintiffs' request for attorneys' fees and expenses, subject to the final judgment. Upon the conclusion of a standard 30-day appeal period, the effective date was deemed to be June 29, 2018. On July 16, 2018, the Company issued and delivered the Settlement Warrants in accordance with the Stipulation and filed a corresponding shelf registration statement to register the shares of common stock underlying the Settlement Warrants which was declared effective by the SEC on July 25, 2018. All 0.2 million Settlement Warrants expired on July 15, 2019 as none of the warrants had been exercised during the one-year exercise period.

The Company evaluates developments in legal proceedings on a quarterly basis. The Company records an accrual for loss contingencies to the extent that the Company concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. In December 2017, upon entering into the MOU, the Company's liability related to this settlement became estimable and probable. Accordingly, the Company recorded an estimated $17.1 million contingent liability, including $15.0 million for the cash portion of the settlement with a corresponding insurance recovery for the 100% portion to be paid directly by certain of the Company's insurance carriers, and an approximate $2.1 million estimate for the warrant portion of the settlement with a corresponding non-cash charge to the Statement of Operations as a component of operating expenses. Pursuant to the Final Judgment, all claims against the Company were released upon the Effective Date. In addition, pursuant to the Stipulation, the Company has no interest in the settlement escrow account subsequent to the Effective Date. Accordingly, the Company reversed the $15.0 million cash portion of the settlement from both the contingent liability and the corresponding insurance recovery as of the Effective Date.

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

Cautionary Note Regarding Forward-Looking Information

This report contains forward-looking statements regarding, among other things, our future development efforts, our collaborations, our future operating results and financial position, our business strategy, our prospects and other objectives for our operations. You can identify these forward-looking statements by their use of words such as "anticipate," "believe," "estimate," "expect," "forecast," "goals," "intend," "may," "might," "plan," "project," "target," "will," "would," "could," "should" and other words and terms of similar meaning, although not all forward-looking statements contain such identifying words. You also can identify them by the fact that they do not relate strictly to historical or current facts. We caution you that there are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by these forward-looking statements. These risks and uncertainties include risks relating to the impact of the COVID-19 pandemic on our clinical trials and other business operations as well as those inherent in pharmaceutical research and development, such as adverse results in our clinical development activities, our ability to obtain any necessary financing to conduct our planned activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our dependence on our existing and future strategic partners, and other risk factors. Please refer to the section entitled "Risk Factors" in Item 1A of Part II and elsewhere in this report for a description of these risks and uncertainties. Unless required by law, we do not undertake any obligation to update any forward-looking statements.

Overview

We are an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. Our strategy is to focus our resources toward development and commercialization of our product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. Our lead candidate is tivozanib FOTIVDA, a vascular endothelial growth factor receptor tyrosine kinase inhibitor, or VEGFR TKI. FOTIVDA is approved through our development partner EUSA Pharma (UK) Limited, or EUSA, in the European Union, or the EU, the United Kingdom, Norway, New Zealand and Iceland for the first-line treatment of adult patients with advanced renal cell carcinoma, or RCC. We are working to develop and potentially commercialize tivozanib in the U.S. as a treatment for RCC and hepatocellular carcinoma, or HCC. In March 2020, we submitted an application for marketing approval, or NDA, to the U.S. Food and Drug Administration, or FDA, for tivozanib as a treatment for relapsed or refractory RCC. In June 2020, the FDA accepted our NDA for substantive review and assigned it a Prescription Drug User Fee Act, or PDUFA, target date of March 31, 2021. We completed an application orientation meeting with the FDA on May 14, 2020 and a mid-cycle review meeting on July 31, 2020. The FDA has conditionally accepted our proposed brand name, FOTIVDA, for tivozanib in the United States. The FDA has also notified us that it does not currently plan to convene an Oncologic Drugs Advisory Committee meeting in connection with its NDA review. In addition to developing tivozanib as a potential monotherapy, and based on tivozanib's demonstrated anti-tumor activity and tolerability profile, we are studying tivozanib in combination with immune checkpoint inhibitors for the treatment of RCC and HCC in phase 2 clinical trials.

Our pipeline of product candidates also includes ficlatuzumab, a hepatocyte growth factor, or HGF, inhibitory monoclonal antibody. We have previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck, or HNSCC, acute myeloid leukemia, or AML, and pancreatic cancer. We are currently conducting a randomized phase 2 confirmatory study of ficlatuzumab for the potential treatment of HNSCC. Our earlier-stage pipeline under development includes AV-203, an anti-ErbB3 monoclonal antibody, as a potential oncology treatment; AV-380, a humanized IgG1 inhibitory monoclonal antibody targeting growth differentiation factor 15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment of cancer cachexia; and AV-353, a monoclonal antibody that targets the Notch 3 pathway, as a potential oncology treatment.

We are committed to creating an environment of diversity and inclusion as a foundation for innovation. We believe that diverse backgrounds and perspectives provide us with better ideas and collaboration across our organization. It is our policy to maintain a work environment free from discrimination based on race, color, religion, national origin, gender, gender identity, transgender status, sexual orientation, age, physical or mental disability, genetic information, veteran status, or marital status.

Business Update Regarding COVID-19. The pandemic caused by an outbreak of a new strain of coronavirus, or the COVID-19 pandemic, that is affecting the U.S. and global economy and financial markets is also impacting our employees, patients, communities and business operations to varying degrees. In the paragraphs that follow, we have described impacts of the COVID-19 pandemic on our clinical development programs, as applicable. The extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. Certain of our operations had been conducted remotely prior to the COVID-19 pandemic, and we have now transitioned essentially all of our business operations to be conducted remotely in response to COVID-19. We have not experienced any material reduction in productivity or interruptions in our general business operations to date. However, if the COVID-19 pandemic continues or becomes more severe, it may impact our ability to maintain that level of productivity, to grow the company as we have anticipated, and to execute our commercialization and other long-term business strategies. Management is actively monitoring this situation and the possible effects on our financial condition, liquidity, operations, suppliers, industry, and workforce. For additional information on risks posed by the COVID-19 pandemic, please see Part II, Item 1A – Risk Factors – Risks Related to the COVID-19 Pandemic, included elsewhere in this Quarterly Report on Form 10-Q.

Tivozanib. Tivozanib is a potent, selective and long half-life inhibitor of all three vascular endothelial growth factor, or VEGF, receptors. It is designed to optimize VEGF blockade while minimizing off-target toxicities, resulting in demonstrated improved anti-tumor activity as compared to the non-selective VEGFR TKI sorafenib, as measured by progression-free survival, or PFS, overall response rate, or ORR, and duration of response, as well as tolerability, as measured by the need for significantly fewer dose reductions and interruptions due to adverse events.

U.S. Marketing Application - Our NDA submission to the FDA is based on our TIVO-3 trial, a phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®) as a third- and fourth-line treatment for RCC, and supported by data from three additional trials, including an active comparator-controlled supportive phase 3 trial, TIVO-1, comparing tivozanib to sorafenib in first-line RCC, and two phase 2 trials, Study 902, the open-label, crossover clinical study of tivozanib for patients who progressed on sorafenib in TIVO-1 and Study 201, a placebo-controlled study in first-line RCC. Our TIVO-3 trial is the first positive phase 3 study in the third- and fourth-line treatment of patients with RCC to meet its primary endpoint, as well as the first phase 3 study in RCC to investigate a predefined subpopulation of patients who received prior checkpoint inhibitor therapy, an emerging standard of care for earlier lines of therapy. Key data from our TIVO-3 trial include the following:

- Tivozanib demonstrated a 44% improvement in median PFS, the primary endpoint, with a median PFS in the tivozanib arm of 5.6 months compared with 3.9 months in the sorafenib arm, and 27% reduction in risk of progression or death compared to sorafenib (hazard ratio (HR)=0.73, p=0.0165).
- ORR for patients receiving tivozanib was 18% compared to 8% for patients receiving sorafenib (p=0.017).
- Median duration of response in patients receiving tivozanib was not reached (95% confidence interval (CI): 12.9, not reached (NR)) and in patients receiving sorafenib was 5.7 months (95% CI: 5.6, NR).
- The final overall survival, or OS, hazard ratio based on a May 1, 2020 cutoff date was 0.97 (p=0.82), and the final median OS was 16.4 months for tivozanib and 19.2 months for sorafenib. The final OS HR of 0.97 was similar to those observed in other Phase 3 studies in RCC comparing a prior FDA-approved VEGFR TKI to another VEGFR TKI..
- Tivozanib also demonstrated a statistically significant improvement in median PFS for the prespecified subgroup of patients (approximately 27% of the patients in the tivozanib arm) who received checkpoint inhibitor therapy in earlier lines of treatment, with a hazard ratio of 0.55 (p=0.028), a 45% reduction in risk of progression or death compared to sorafenib, and a median PFS in the tivozanib arm of 7.3 months compared with 5.1 months in the sorafenib arm. The ORR for patients in this subgroup receiving tivozanib was 24.4% compared to 6.8% receiving sorafenib. The final OS hazard ratio for this subgroup was 0.84.
- Tivozanib was generally better tolerated than sorafenib with significantly fewer dose reductions and interruptions due to adverse events. In the tivozanib arm, 46% of patients experienced Grade 3 or higher adverse events compared to 55% of patients in the sorafenib arm. Infrequent but severe adverse events reported in greater number in the tivozanib arm were thrombotic events similar to those observed in previous tivozanib studies. The most common adverse event in patients receiving tivozanib was hypertension, an adverse event known to reflect effective VEGF pathway inhibition, which has shown a correlation with better PFS outcomes.

We believe there is significant potential commercial opportunity for tivozanib in the United States if it is approved by the FDA. We estimate that the current U.S. market for relapsed or refractory RCC therapy is approximately $1.0 billion, including $700 million in the second line and $300 million in the third and fourth lines. As the TIVO-3 study is the first positive phase 3 study in third and fourth line RCC, we believe that, if approved, tivozanib can become a standard of care.

We continue to rapidly build our commercial infrastructure in preparation for the potential commercialization of tivozanib in the U.S. In the third quarter, we have continued to expand our medical affairs, sales, marketing, market access and distribution capabilities and teams. In light of the restrictions necessitated by the COVID-19 pandemic, we are designing our strategic commercial approach to be optimized for remote as well as in-person customer engagement capabilities, as well as expanding our digital marketing strategies.

Combination Development - In addition to the development of tivozanib as a single agent, we have clinical collaborations to study tivozanib in combination with immune checkpoint inhibitors in RCC and HCC. We sponsored the TiNivo trial, a phase 1b/2 clinical trial of tivozanib in combination with Opdivo® (nivolumab), an immune checkpoint (PD-1) inhibitor, in the first- and second-line treatment of RCC, for which Bristol-Myers Squibb supplied nivolumab. The combination required few dose reductions and showed additive or synergistic activity for ORR and PFS in both treatment naïve and previously treated patients with RCC. Out of 25 patients who were treated with the full dose and schedule of oral tivozanib in combination with intravenous nivolumab, thirteen (52%) had received at least one prior systemic therapy, including two (8%) that had received prior checkpoint inhibitor therapy, and twelve (48%) that were treatment naïve. The overall median PFS for the 25 patients was 18.9 months. Outcomes were comparable in the treatment naïve and prior treatment patients suggesting no loss of activity for the combination following prior treatment. The median PFS for the twelve previously untreated patients was 18.9 months and the median PFS for the thirteen previously treated patients had not yet been achieved as of the final data cut-off date of August 27, 2019. An ORR was observed in 14 patients (56%) (complete response plus partial response), including one treatment naïve patient (4%) achieving a complete response, and a disease control rate (complete response plus partial response plus stable disease) was observed in 24 patients (96%). Of the two patients (8%) who received prior PD-1 therapy, one achieved a partial response and the other achieved stable disease. Treatment-related Grade 3/4 adverse events occurred in 80% of patients, the most common of which was hypertension, and only 17% of patients required a dose reduction. In September 2019, we presented final PFS results of our TiNivo trial at the European Society for Medical Oncology 2019 Congress. Based on these results from the TiNivo trial, we are currently evaluating opportunities to continue to develop tivozanib with an immune checkpoint inhibitor in RCC.

We are also sponsoring the DEDUCTIVE trial in collaboration with AstraZeneca PLC, or AstraZeneca. The DEDUCTIVE trial is an open-label, multi-center, randomized phase 1b/2 clinical trial of tivozanib in combination with IMFINZI (durvalumab), AstraZeneca’s monoclonal antibody directed against programmed death-ligand 1, or PD-L1, in the first-line treatment of patients with advanced, unresectable HCC who have not received prior systemic therapy. Pursuant to our clinical supply agreement with an affiliate of AstraZeneca. we serve as the study sponsor, each party contributes the clinical supply of its study drug and external study costs are otherwise shared equally. The DEDUCTIVE trial has progressed to phase 2 following the successful completion of the phase 1b portion of the trial, where 1.0 mg of tivozanib was administered for 21 days followed by seven days off treatment together with 1,500 mg of durvalumab every 28 days. The combination was well-tolerated, with no dose limiting toxicities. We expect to enroll up to an additional 30 patients in the phase 2 expansion portion of the trial at the dose and schedule designated in the phase 1b portion. The primary outcome measure of the DEDUCTIVE trial is incidence of treatment emergent adverse events and the secondary outcome measures include ORR, PFS and OS. We expect to present preliminary data from the trial at a scientific meeting in the first half of 2021.

All of the clinical trial sites have been initiated for the DEDUCTIVE trial. At certain sites enrollment has been suspended at times due to COVID-19 related restrictions. In addition, some patients may have difficulty accessing clinical trial sites or attending appointments due to COVID-19 related health and safety concerns and restrictions, and healthcare resources may be diverted from the conduct of our trial in order to focus on pandemic concerns. Accordingly, enrollment has proceeded at a slower pace than forecasted prior to the onset of the pandemic, and we cannot guarantee the future pace of enrollment. Further, certain trial functions, including trial monitoring, will continue to be conducted remotely where possible. We do not yet know whether remote management of these functions will prove to be sufficient. We have sufficient clinical supply of tivozanib manufactured to complete the DEDUCTIVE trial. The DEDUCTIVE trial also requires treatment with durvalumab, which is administered intravenously and supplied by AstraZeneca. Any interruptions in the supply or delivery of study drug for the trial would impact patient treatment. The extent and impact of any future disruptions on enrollment, patient treatment and trial management of our DEDUCTIVE trial due to the COVID-19 pandemic are uncertain and may change with the local and global fluctuations in the incidence of COVID-19.

KKC License and Non-Oncology Development - We licensed our rights to tivozanib from Kyowa Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KKC, in December 2006. Pursuant to our license agreement with KKC, or the KKC Agreement, we obtained an exclusive, sublicensable license to develop, manufacture and commercialize tivozanib worldwide except for Asia and the Middle East, where KKC retained the rights to tivozanib. We have no remaining development and commercialization milestone payments due to KKC under this agreement. We have royalty payment obligations to KKC related to our oncology development of tivozanib in our territory, which range from the low to mid-teens as a percentage of net sales. We are also required to pay KKC 30% of amounts we receive from our European, or any other, sublicensee, subject to certain exceptions and limitations.

In August 2019, KKC repurchased the non-oncology rights to tivozanib from us in our territory (excluding the rights we have sublicensed to EUSA, as described below). In connection with this repurchase, KKC paid us a $25.0 million upfront fee and waived a one-time milestone payment of $18.0 million otherwise payable by us upon our obtaining marketing approval for tivozanib in the U.S. In August 2020, KKC paid us a $2.8 million development milestone upon acceptance by the Pharmaceuticals and Medical Devices Agency of Japan of KKC's investigational new drug application, or IND, for a non-oncology formulation of tivozanib. KKC has milestone payment obligations to us of up to an aggregate of $390.7 million upon the achievement of certain development and sales milestones. KKC also has royalty payment obligations related to non-oncology sales in our territory ranging from high single digits to low double digits as a percentage of net sales.

<u>EUSA Sublicense and Commercialization</u> - We have sublicensed tivozanib to EUSA in Europe and other territories outside of North America. In August 2017, the European Commission granted marketing authorization to EUSA for tivozanib in all 28 countries of the EU, including the United Kingdom, Norway and Iceland. Tivozanib, sold under the brand name FOTIVDA, is approved for the first-line treatment of adult patients with RCC and for those who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. EUSA has received reimbursement approval and commercially launched FOTIVDA in Germany, the United Kingdom and Spain as well as in additional countries. Tivozanib has also been approved in South Africa and New Zealand. Under our license agreement with EUSA, or the EUSA Agreement, we are eligible to receive regulatory and sales milestone payments as well as tiered double-digit royalties on EUSA's annual net sales of FOTIVDA ranging from a low double digit up to mid-twenty percent. We began earning sales royalties upon EUSA's first commercial launch of FOTIVDA with the initiation of product sales in Germany in November 2017. We are also eligible to receive a research and development reimbursement from EUSA of $20 million of our total TIVO-3 trial costs if EUSA chooses to opt-in to use the TIVO-3 dataset to seek an expanded RCC indication in the EU, or for other regulatory or commercialization purposes. The leadership of EUSA has informed us that it is interested in seeking an expanded label, but has requested to more closely align the payment stream under which it would satisfy its $20 million reimbursement obligation with the occurrence of the incremental value creation for EUSA. We are currently in negotiations with EUSA regarding the structuring of this payment stream. We cannot be certain that we will arrive at mutually acceptable terms, or that EUSA will ultimately exercise the opt-in.

EUSA has reported to us that to date, it has not experienced a decrease in sales trends or interruptions in supply or distribution of FOTIVDA during the COVID-19 pandemic; however, the future impact of the COVID-19 pandemic on FOTIVDA sales is difficult to predict.

Ficlatuzumab. Ficlatuzumab is a potent HGF inhibitory antibody. HGF is the sole known ligand of the c-Met receptor, which is believed to trigger many activities that are involved in cancer development and metastasis. We have seen promising results for ficlatuzumab as a potential treatment of HNSCC, AML, and pancreatic cancer in early clinical trials. The estimated number of annual new cases of head and neck cancer, AML and pancreatic cancer in the United States is 57,600, 53,260 and 19,940, respectively (American Cancer Society, Cancer Facts & Figures 2020). In September 2020, we made the decision to fund additional clinical manufacturing of ficlatuzumab to enable a potential registrational Phase 3 clinical trial in HNSCC after final results from the open-label, randomized Phase 2 study are available, as well as to enable additional potential development in Phase 2 studies in pancreatic cancer and AML.

We and Biodesix, Inc., or Biodesix, funded an investigator-sponsored phase 1 clinical trial of ficlatuzumab in combination with cetuximab in HNSCC. In June 2017, preliminary results of the phase 1 trial were presented and showed that ficlatuzumab in combination with cetuximab in patients with cetuximab-resistant, metastatic HNSCC was well tolerated, resulted in a disease control rate of 67% and demonstrated activity prolonging PFS and OS compared to historical controls of cetuximab alone. We and Biodesix are funding an investigator-sponsored multi-center randomized phase 2 trial of ficlatuzumab in ERBITUX® (cetuximab) refractory patients in HNSCC to confirm these findings and to explore other markers of activity.

The phase 2 trial is being conducted under the direction of Julie E. Bauman, MD, MPH, Chief, Division of Hematology/Oncology at the University of Arizona Cancer Center. The trial is designed to enroll approximately 60 patients randomized to receive either ficlatuzumab alone or ficlatuzumab and cetuximab, and enrollment is expected to be complete in the fourth quarter of 2020. We expect to receive top line data from the trial in the first half of 2021. We are evaluating opportunities to initiate a phase 3 clinical trial of ficlatuzumab for the treatment of HNSCC in 2022.

In January 2020, we announced results from an investigator-sponsored trial of ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer. The trial was designed to determine maximum tolerated dose of ficlatuzumab when combined with gemcitabine and nab-paclitaxel. Secondary outcome measures include response rate and PFS. A total of 24 patients enrolled in the trial and the average number of 28-day treatment cycles received was 7.5 (range 1-15), with three patients remaining on active treatment at the end of the trial. The combination showed a promising ORR and disease control rate relative to data observed for gemcitabine and nab-paclitaxel alone. Treatment with this regimen was associated with significant hypoalbuminemia and edema, and therefore a follow-up safety study is under consideration to evaluate ficlatuzumab in combination with an alternate cytotoxic regimen.

We and Biodesix have also funded an investigator-sponsored phase 1b/2 clinical trial of ficlatuzumab in combination with cytarabine in AML, which we refer to as the CyFi-1 trial, which showed a favorable complete response rate in the 18 primary refractory AML patients enrolled in the trial and an acceptable tolerability profile. Based on the encouraging findings from the CyFi-1 trial, we and Biodesix designed a randomized phase 2 clinical trial evaluating ficlatuzumab in combination with high-dose cytarabine versus high-dose cytarabine alone in patients with AML, which we referred to as the CyFi-2 trial. However, in March 2020, we discontinued the CyFi-2 trial prior to the initiation of patient enrollment due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial drug supply.

In September 2020, we regained full global rights to ficlatuzumab, as a result of our former development partner Biodesix exercising its Opt-Out rights (as defined below) under the Co-Development and Collaboration Agreement, or the Biodesix Agreement, dated April 9, 2014, as amended, by and between us and Biodesix. The Biodesix Agreement generally provided for each party to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab and to share equally in any future revenue from development or commercialization. Under the Biodesix Agreement, prior to the first commercial sale of ficlatuzumab, each party had the right to elect to discontinue its funding obligation for further development or commercialization efforts with respect to ficlatuzumab in exchange for reduced economics in the program, which is referred to as an "Opt-Out." Pursuant to the terms of the Biodesix Agreement, as a result of Biodesix's election to Opt-Out, Biodesix will (i) continue to be responsible for reimbursement of development costs with respect to the ongoing Phase 2 investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC, (ii) cease to be entitled to 50% sharing of profits resulting from commercialization of ficlatuzumab, (iii) be entitled to a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses), less approximately $2.5 million Biodesix would be required to pay to us pursuant to the October 2016 amendment to the Biodesix Agreement and (iv) remain responsible for development obligations under the Biodesix Agreement with respect to VeriStrat®. We and Biodesix also remain obligated to negotiate a commercialization agreement to delineate our respective rights and obligations in the event of any commercialization of VeriStrat® with ficlatuzumab. As a result of Biodesix's decision to Opt-Out, we now have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. The Biodesix Agreement will remain in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

AV-203. AV-203 is a potent anti-ErbB3 (also known as HER3) specific monoclonal antibody with high ErbB3 affinity. We have partnered with CANbridge Life Sciences Ltd., or CANbridge, to develop, manufacture and commercialize AV-203 in all countries outside of North America under a collaboration and license agreement. We have retained the North American rights to AV-203. We are eligible to receive from CANbridge certain milestone payments and upon commercialization, tiered royalties on net sales, subject to a sublicense fee to Biogen Idec International GmbH, or Biogen. CANbridge has advised us that it is evaluating NRG1 Fusion biomarker directed development plans with the potential to initiate a clinical study in 2021. NRG1 Fusions, which are certain alterations in the NRG1 gene that may cause increased levels of the growth factor NRG1, are a potential biomarker for response to AV-203 in various tumor types.

AV-380. AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting GDF15, a divergent member of the TGF-ß family. We are developing AV-380 for the potential treatment or prevention of cachexia. Cachexia is defined as a multi-factorial syndrome of involuntary weight loss characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. It is estimated that cachexia affects approximately 9 million individuals in North America, Europe and Japan (J Cachexia Sarcopenia Muscle 2010). Cachexia is associated with various cancers, and it is estimated that approximately 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present (J Cachexia Sarcopenia Muscle 2010). We believe AV-380 has the potential to address a significant unmet need. Cachexia also affects patients with chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, anorexia nervosa and other diseases.

We believe that AV-380 represents a unique approach to treating cachexia because it has been demonstrated in preclinical studies to address key underlying mechanisms of the syndrome. Our research suggests that greater than 70% of cancer patients have increased GDF15 expression, starting at the pre-cachectic stage. If GDF15 inhibitors such as AV-380 are proven clinically successful, we believe there is a significant market opportunity with potential application in multiple tumor types in combination with multiple anti-cancer treatment standards. In addition to our patents and patent applications covering our proprietary AV-380 antibody program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital Sydney Limited in Sydney, Australia, which we refer to as St. Vincent's. We have milestone and royalty payment obligations under our license agreement with St. Vincent's.

We have completed preclinical toxicology studies designed to support an IND filing for AV-380 with the FDA, which we plan to submit in the fourth quarter of 2020. We are planning to initiate a phase 1 trial in the first quarter of 2021 if our IND submission is accepted.

AV-353. AV-353 is a potent inhibitory monoclonal antibody specific to Notch 3. The Notch 3 pathway is important in cell-to-cell communication involving gene regulation mechanisms that control multiple cell differentiation processes during the entire life cycle. Scientific literature has implicated the Notch 3 receptor pathway in multiple diseases, including cancer, cardiovascular diseases, such as pulmonary arterial hypertension, and neurodegenerative conditions. We are currently evaluating options to develop AV-353 in oncology indications.

We do not have a history of generating operating profits and, as of September 30, 2020, we had an accumulated deficit of $609.7 million. Our revenue was $5.1 million and $28.0 million in the nine months ended September 30, 2020 and 2019, respectively. We recorded an operating loss of $26.2 million in the nine months ended September 30, 2020 and operating income of $6.3 million in the nine months ended September 30, 2019. We recorded a net loss of $24.1 million in the nine months ended September 30, 2020 and net income of $13.8 million in the nine months ended September 30, 2019. Our net income in the nine months ended September 30, 2019 was attributable to license revenue recognized during the period as well as other income recognized related to the change in fair value of the PIPE Warrants as described further within this Management's Discussion and Analysis of Financial Condition and Results of Operations. We anticipate that we will continue to incur significant operating losses over the next several years as we continue our planned development activities for our preclinical and clinical stage assets and conduct commercial launch-readiness initiatives in support of a possible commercial launch of tivozanib in RCC.

Going Concern

As of November 9, 2020, the date of issuance of these unaudited condensed consolidated financial statements, we believe that our cash, cash equivalents and marketable securities of $68.8 million as of September 30, 2020 will not be sufficient to fund our current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q. Consequently, in accordance with the requirements of Accounting Standards Update, or ASU, No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Accounting Standards Codification, or ASC, Subtopic 205-40), or ASC 205-40, we have determined that there is substantial doubt about our ability to continue as a going concern. To continue as a going concern, we must secure additional funding to support our current operating plan. For more information, refer to "*Liquidity and Capital Resources—Liquidity and Going Concern*" below, as well as Note 1, "*—Liquidity and Going Concern*" of the Notes to our condensed consolidated financial statements and "— Risk Factors –*We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern*," each included elsewhere in this Quarterly Report on Form 10-Q.

Financial Overview

We do not have a history of being profitable and, as of September 30, 2020, we had an accumulated deficit of $609.7 million. We anticipate that we will continue to incur significant operating losses over the next several years as we continue our planned development activities for our preclinical and clinical stage assets and conduct commercial launch-readiness initiatives in support of a possible commercial launch of tivozanib in RCC.

We will require substantial additional funding to continue our planned operating activities, and the timing and nature of activities contemplated for the remainder of 2020 and thereafter will be conducted subject to the availability of sufficient financial resources. Refer to the "Liquidity and Capital Resources—Liquidity and Going Concern" section for a further discussion of our funding requirements.

Revenue

Our revenues have historically been generated primarily through collaborative research, development and commercialization agreements. Payments to us under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales. In November 2017, we began earning sales royalties upon EUSA's commencement of the first commercial launch of tivozanib (FOTIVDA).

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. In March 2020, we submitted an NDA to the FDA for tivozanib as a treatment for relapsed or refractory RCC if approved by the FDA. In June 2020, the FDA accepted our NDA for substantive review and assigned it a PDUFA target date of March 31, 2021. We expect that any revenue we generate will fluctuate from quarter to quarter and year to year as a result of the timing and amount of license fees, research and development reimbursements, milestones, royalties and other payments received under our strategic partnerships, and the payments that we receive upon the sale of our products, to the extent any are successfully commercialized. If we or our strategic partners fail to complete the development of our drug candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Research and development expenses have historically consisted of expenses incurred in connection with the discovery and development of our product candidates. We recognize research and development expenses as they are incurred. These expenses consist primarily of:

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation and research-related overhead;
- external development-related expenses, including clinical trials, preclinical studies, consultants and other outsourced services;
- costs of acquiring and manufacturing drug development related materials and related distribution;
- costs associated with our regulatory and quality assurance operations and medical affairs;
- upfront license payments, milestones, sublicense fees and royalties related to in-licensed products and technology; and
- allocated expenses for facilities and information technology.

Research and development expenses are net of amounts reimbursed under our agreements with EUSA, Biodesix, and AstraZeneca for their respective shares of development costs incurred by us under our joint development plans with each respective partner.

We anticipate that research and development expenses will remain consistent at current levels through the first half of 2021 and increase in the second half of 2021, principally related to the timing of ficlatuzumab GMP drug manufacturing. We anticipate that increases in research and development expenses in 2021, principally related to a full year of costs for ficlatuzumab drug manufacturing and the medical affairs function in support of a potential commercial launch of tivozanib, if approved by the FDA, will be partially offset by lower costs, principally related to the TIVO-3 trial that is expected to be closed following the FDA's March 31, 2021 PDUFA target date for our tivozanib NDA and costs incurred in 2020 that will not be incurred in 2021 related to the submission of our tivozanib NDA on March 31, 2020 and the completion of AV-380 pre-clinical development. Accordingly, the timing and nature of contemplated activities during the remainder of 2020 and in 2021 will be conducted subject to the availability of sufficient financial resources.

Currently, we track direct external development expenses and direct salary on a program-by-program basis and allocate general-related expenses, such as indirect compensation, benefits and consulting fees, to each program based on the personnel resources allocated to such program. Facilities, IT costs and stock-based compensation are not allocated amongst programs and are considered overhead.

Uncertainties of Estimates Related to Research and Development Expenses

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval for each of our product candidates is costly and time-consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the risk benefit profile of the product candidates' clinical activity, investment in the program, competition, manufacturing capabilities and commercial viability.

At this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates, or the period, if any, in which material net cash inflows may commence from sales of any approved products. This uncertainty is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- our ability to establish and maintain strategic partnerships, the terms of those strategic partnerships and the success of those strategic partnerships, if any, including the timing and amount of payments that we might receive from strategic partners;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any product candidate;
- the progress and results of our clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the emergence of competing technologies and products and other adverse market developments;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; and
- additional manufacturing requirements.

As a result of the uncertainties associated with developing drugs, including those discussed above, we are unable to determine the exact duration and completion costs of current or future clinical stages of our product candidates, or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success, if any, of each product candidate, as well as ongoing assessment of each product candidate's commercial potential. We will need to raise substantial additional capital in the future in order to fund the development of our preclinical and clinical product candidates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of compensation, benefits and travel for employees in executive, finance, legal, human resource and commercial functions. Other selling, general and administrative expenses include professional fees for audit, tax, general legal, patent legal, investor relations, commercial, consulting services and directors' fees, as well as facility and information technology-related costs not otherwise included in research and development expenses.

As we approach our PDUFA target date, we anticipate that selling, general and administrative expenses will continue to increase significantly through a potential commercial launch of tivozanib, if approved by the FDA, and will remain consistent at that level in the second half of 2021, principally related to our sales, marketing, market access and distribution teams and capabilities, and general and administrative support. Accordingly, the timing and nature of contemplated activities during the remainder of 2020 and in 2021 will be conducted subject to the availability of sufficient financial resources.

Warrants Issued in Connection with Private Placement

In May 2016, we issued warrants to purchase an aggregate of 1,764,242 shares of our common stock in connection with a private placement financing, which we refer to herein as the PIPE Warrants. As of September 30, 2020, PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding. No PIPE Warrants were exercised during each of the three and nine months ended September 30, 2020 and 2019. Refer to"—Liquidity and Capital Resources—Private Placement/PIPE Warrants" below and Note 3, "*Significant Accounting Policies - Warrants Issued in Connection with Private Placement*" to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

The PIPE Warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net until the earlier of their exercise or expiration or upon the completion of a liquidation event. Upon exercise, the PIPE Warrants are subject to revaluation just prior to the date of exercise and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net and the corresponding reduction in the warrant liability is recorded as additional paid-in capital in the Balance Sheet as a component of stockholder's equity.

The key assumptions used to value the PIPE Warrants in the three months and nine months ended September 30, 2020 were as follows:

	December 31, 2019	March 31, 2020	June 30, 2020	September 30, 2020
Expected price volatility	133.07%	153.37%	108.20%	103.29%
Expected term (in years)	1.50	1.25	1.00	0.75
Risk-free interest rates	1.59%	0.17%	0.16%	0.12%
Stock price	$ 6.20	$ 3.62	$ 5.15	$ 5.94
Dividend yield	—	—	—	—

The key assumptions used to value the PIPE Warrants in the three months and nine months ended September 30, 2019 were as follows:

	December 31, 2018	March 31, 2019	June 30, 2019	September 30, 2019
Expected price volatility	82.64%	111.99%	113.86%	119.11%
Expected term (in years)	2.50	2.25	2.00	1.75
Risk-free interest rates	2.47%	2.27%	1.75%	1.63%
Stock price	$ 16.00	$ 8.20	$ 6.70	$ 8.40
Dividend yield	—	—	—	—

Interest Expense, Net

Interest expense consists of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable, and is shown net of interest income, which consists of interest earned on our cash, cash equivalents and marketable securities. The primary objective of our investment policy is capital preservation.

Income Taxes

We calculate our provision for income taxes on ordinary income based on our projected annual tax rate for the year. As of September 30, 2020, we are forecasting an effective tax-rate of 0% for the year ending December 31, 2020, and since we maintain a full valuation allowance on all of our deferred tax assets, we have recorded no income tax provision or benefit in the current quarter.

Significant Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, the measurement of right-of-use assets and lease liabilities, the assessment of our ability to continue as a going concern, and the reported amounts of revenues and expenses during the reported periods. On an ongoing basis, we evaluate our estimates and judgments for changes in facts and circumstances, including those related to revenue recognition, contract research accruals, measurements of the PIPE Warrant liability, stock-based compensation, and estimates of our capital requirements over the next twelve months from the date of issuance of the interim condensed consolidated financial statements. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in our disclosures in the period in which they become known. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate. Our significant accounting policies are described in the notes to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. During the three months and nine months ended September 30, 2020, there were no material changes to our significant accounting policies and significant judgments and estimates as reported in our Annual Report on Form 10-K for the year ended December 31, 2019, which we filed with the Securities and Exchange Commission, or SEC, on March 16, 2020.

Recent Accounting Pronouncements

For a discussion of recent accounting pronouncements, refer to Note 3 – *"Significant Accounting Policies—Recently Adopted Accounting Pronouncements",* to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Results of Operations

Comparison of Three Months and Nine Months Ended September 30, 2020 and 2019

Revenues (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2020	**2019**	**$**	**%**	**2020**	**2019**	**$**	**%**
KKC	2,800	25,000	(22,200)	(89)%	2,800	25,000	(22,200)	(89)%
EUSA	800	717	83	12%	2,333	3,031	(698)	(23)%
Total	$ 3,600	$ 25,717	$ (22,117)	(86)%	$ 5,133	$ 28,031	$ (22,898)	(82)%

Our total partnership revenues decreased by $22.1 million, or 86%, to $3.6 million in the three months ended September 30, 2020 from $25.7 million in the three months ended September 30, 2019, principally due to payments we earned pursuant to the amendment to the KKC Agreement for KKC's repurchase of the non-oncology rights to tivozanib in our territory, including the $25.0 million upfront payment we earned in the third quarter of 2019 offset by a $2.8 million development milestone we earned in the third quarter of 2020.

On August 1, 2019, we entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in our territory, excluding the rights we have sublicensed to EUSA under the EUSA Agreement, and KKC made a $25.0 million non-refundable upfront payment to us that we received in September 2019. In the third quarter of 2019, we recognized this $25.0 million upfront payment as revenue in accordance with ASC 606. On August 2, 2020, we earned a $2.8 million development milestone payment from KKC for the acceptance of KKC's IND for a non-oncology formulation of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan. In the third quarter of 2020, we recognized this $2.8 million development milestone as revenue in accordance with ASC 606. Prior to the amendment to the KKC Agreement, KKC did not have any payment obligations to us for non-oncology rights to tivozanib in our territory. Refer to Note 4 *"Collaborations and License Agreements* – KKC", to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q regarding the specific application of ASC 606 to our amendment to the KKC Agreement.

Our total partnership revenues decreased by $22.9 million, or 82%, to $5.1 million in the nine months ended September 30, 2020 from $28.0 million in the nine months ended September 30, 2019, principally due to payments we earned pursuant to the amendment to the KKC Agreement for KKC's repurchase of the non-oncology rights to tivozanib in our territory, including the $25.0 million upfront payment we earned in the nine months ended September 30, 2019 offset by a $2.8 million development milestone we earned in the nine months ended September 30, 2020, as well as a $1.0 million decrease related to revenue recognized in connection with a milestone payment we earned from EUSA in February 2019 that was not recognized in the nine months ended September 30, 2020.

In February 2019, we earned a $2.0 million milestone payment under the EUSA Agreement for reimbursement approval for tivozanib (FOTIVDA) in the first-line treatment of RCC from the Ministry of Health, Consumer Affairs and Social Welfare in Spain. In accordance with ASC 606, we recognized $1.0 million in revenue in the nine months ended September 30, 2019 that was not recognized in the nine months ended September 30, 2020. No milestone payments were earned under the EUSA Agreement in the nine months ended September 30, 2020. Refer to Note 4 *"Collaborations and License Agreements* – EUSA", to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q regarding the specific application of ASC 606 *Revenue from Contracts with Customers* to our EUSA Agreement.

Research and Development Expenses (in thousands)

	Three Months Ended September 30, 2020	Three Months Ended September 30, 2019	Comparison $	Comparison %	Nine Months Ended September 30, 2020	Nine Months Ended September 30, 2019	Comparison $	Comparison %
Tivozanib	$ 4,796	$ 2,946	$ 1,850	63%	$ 14,160	$ 9,043	$ 5,117	57%
AV-380 Program in Cachexia	524	208	316	152%	1,938	2,691	(753)	(28)%
Ficlatuzumab	133	439	(306)	(70)%	878	675	203	30%
Overhead	407	390	17	5%	1,129	1,037	92	9%
Total research and development expenses	$ 5,860	$ 3,983	$ 1,877	47%	$ 18,105	$ 13,446	$ 4,659	35%

Our total research and development expenses increased by $1.9 million, or 47%, to $5.9 million in the three months ended September 30, 2020 from $4.0 million in the three months ended September 30, 2019, principally due to a $1.9 million increase in tivozanib-related expenses.

Our total research and development expenses increased by $4.7 million, or 35%, to $18.1 million in the nine months ended September 30, 2020 from $13.4 million in the nine months ended September 30, 2019, principally due to increases of $5.1 million in tivozanib-related expenses and $0.2 million in ficlatuzumab-related expenses, partially offset by a decrease of $0.8 million in AV-380 related expenses.

Tivozanib expenses increased by $1.9 million, or 63%, in the three months ended September 30, 2020 as compared to the three months ended September 30, 2019, principally due to increases totaling $2.6 million, partially offset by a $0.7 million decrease related to lower expenses in connection with the TIVO-3 and TiNivo trials that are nearing completion. The $2.6 million in total increases principally included: (i) $0.3 million related to the ongoing support of the FDA's review of the NDA, and (ii) $2.2 million in commercial launch-readiness initiatives incurred in the three months ended September 30, 2020 that were not incurred in the three months ended September 30, 2019, including $1.7 million related to the conduct of certain post-commercial launch drug supply manufacturing, $0.4 million related to the buildout of our medical affairs function and $0.1 million related to other commercial-launch readiness initiatives.

Tivozanib expenses increased by $5.1 million, or 57%, in the nine months ended September 30, 2020 as compared to the nine months ended September 30, 2019. The $5.1 million increase was principally due to increases totaling $7.2 million, partially offset by decreases totaling $2.2 million. The $7.2 million in total increases principally included: (i) $4.1 million related to the tivozanib NDA for RCC, including $1.2 million related to the completion of the NDA submission and ongoing support of the FDA's review of the NDA and the $2.9 million application user fee pursuant to the PDUFA that was due upon the filing of the tivozanib NDA on March 31, 2020, (ii) $0.5 million related to the DEDUCTIVE trial that was initiated in September 2019, net of cost sharing with AstraZeneca, and (iii) $2.5 million in commercial launch-readiness initiatives incurred in the nine months ended September 30, 2020 that were not incurred in the nine months ended September 30, 2019, including $1.7 million related to the conduct of certain post-commercial launch drug supply manufacturing, $0.7 million related to the buildout of our medical affairs function and $0.1 million related to other commercial-launch readiness initiatives.

These increases were partially offset by decreases totaling $2.2 million, principally including $1.6 million related to lower expenses in connection with the TIVO-3 and TiNivo trials that are nearing completion and $0.6 million related to sublicense fees due to KKC incurred in the first quarter of 2019 in connection with a milestone we earned under our EUSA Agreement that were not incurred in the nine months ended September 30, 2020.

AV-380 expenses increased by $0.3 million, or 152%, in the three months ended September 30, 2020 as compared to the three months ended September 30, 2019 principally due to pre-clinical development costs incurred in the third quarter of 2020 that were not incurred in the third quarter of 2019.

AV-380 expenses decreased by $0.8 million, or 28%, in the nine months ended September 30, 2020 as compared to the nine months ended September 30, 2019. The $0.8 million decrease was principally due to the $2.3 million time-based milestone obligation due to St. Vincent's in the first quarter of 2019 that was not incurred in the nine months ended September 30, 2020, partially offset by an increase of $1.5 million related to pre-clinical development costs incurred in the nine months ended September 30, 2020 that were not incurred in the nine months ended September 30, 2019.

Ficlatuzumab expenses decreased by $0.3 million, or 70%, in the three months ended September 30, 2020 as compared to the three months ended September 30, 2019. The $0.3 million decrease was due to start-up costs incurred in the third quarter of 2019, net of cost sharing with Biodesix, that were not incurred in the third quarter of 2020 in connection with the CyFi-2 trial that was initiated in November 2019. In March 2020, we decided to discontinue the CyFi-2 trial due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, as described above under "Overview – Ficlatuzumab."

Ficlatuzumab expenses increased by $0.2 million, or 30%, in the nine months ended September 30, 2020 as compared to the nine months ended September 30, 2019. The $0.2 million increase was due to start-up costs incurred in the nine months ended September 30, 2020, net of cost sharing with Biodesix, that were not incurred in the nine months ended September 30, 2019 in connection with the CyFi-2 trial that was initiated in November 2019 and discontinued in March 2020, as highlighted above.

We anticipate that research and development expenses will remain consistent at current levels through the first half of 2021 and increase in the second half of 2021, principally related to the timing of ficlatuzumab GMP drug manufacturing. We anticipate that increases in research and development expenses in 2021, principally related to a full year of costs for ficlatuzumab drug manufacturing and the medical affairs function in support of a potential commercial launch of tivozanib, if approved by the FDA, will be partially offset by lower costs, principally related to the TIVO-3 trial that is expected to be closed following the FDA's March 31, 2021 PDUFA target date for our tivozanib NDA and costs incurred in 2020 that will not be incurred in 2021 related to the submission of our tivozanib NDA on March 31, 2020 and the completion of AV-380 pre-clinical development. Accordingly, the timing and nature of contemplated activities during the remainder of 2020 and in 2021 will be conducted subject to the availability of sufficient financial resources.

Selling, General and Administrative Expenses (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2020	2019	$	%	2020	2019	$	%
Selling, general and administrative expenses	$ 5,800	$ 2,884	$ 2,916	101%	13,209	8,325	4,884	59%

Selling, general and administrative expenses increased by $2.9 million, or 101%, to $5.8 million in the three months ended September 30, 2020 from $2.9 million in the three months ended September 30, 2019. The $2.9 million increase was principally due to: (i) $2.3 million in commercial launch-readiness initiatives incurred in the three months ended September 30, 2020 that were not incurred in the three months ended September 30, 2019, including $0.9 million in compensation costs related to the growth in our commercial infrastructure and $1.4 million related to external commercial-launch readiness activities in marketing, market access and commercial operations, (ii) $0.5 million in other professional fees, and (iii) $0.1 million in other compensation-related costs.

Selling, general and administrative expenses increased by $4.9 million, or 59%, to $13.2 million in the nine months ended September 30, 2020 from $8.3 million in the nine months ended September 30, 2019. The $4.9 million increase was principally due to: (i) $3.4 million in commercial launch-readiness initiatives incurred in the nine months ended September 30, 2020 that were not incurred in the nine months ended September 30, 2019, including $1.5 million in compensation costs related to the growth in our commercial infrastructure and $1.9 million related to external commercial-launch readiness activities in marketing, market access and commercial operations, (ii) $1.3 million in other professional fees, and (iii) $0.3 million in other compensation-related costs.

As we approach our PDUFA target date, we anticipate that selling, general and administrative expenses will continue to increase significantly through a potential commercial launch of tivozanib, if approved by the FDA, and will remain consistent at that level in the second half of 2021, principally related to our sales, marketing, market access and distribution teams and capabilities, and general and administrative support. Accordingly, the timing and nature of contemplated activities during the remainder of 2020 and in 2021 will be conducted subject to the availability of sufficient financial resources.

Change in Fair Value of PIPE Warrant Liability (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2020	2019	$	%	2020	2019	$	%
Change in fair value of PIPE Warrant liability	$ 86	$ (1,954)	$ 2,040	(104)%	$ 3,184	$ 9,071	$ (5,887)	(65)%

In May 2016, we issued the PIPE Warrants in connection with a private placement financing and recorded the warrants as a liability. The PIPE Warrants are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in our Statement of Operations as a component of other income (expense).

In the three months ended September 30, 2020, we recorded an approximate non-cash gain of $0.1 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that resulted from a decrease in our stock volatility rate and the shorter remaining term as the PIPE Warrants approach expiration in May 2021, partially offset by a higher stock price of $5.94 on September 30, 2020 compared to the stock price of $5.15 on June 30, 2020.

In the nine months ended September 30, 2020, we recorded an approximate non-cash gain of $3.2 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that resulted from a lower stock price of $5.94 on September 30, 2020 compared to the stock price of $6.20 on December 31, 2019, as well as a decrease in our stock volatility rate and the shorter remaining term as the PIPE Warrants approach expiration in May 2021.

In the three months ended September 30, 2019, we recorded an approximate non-cash loss of $2.0 million in our Statement of Operations attributable to the increase in the fair value of the PIPE Warrant liability that principally resulted from a higher stock price of $8.40 on September 30, 2019 compared to the stock price of $6.70 on June 30, 2019.

In the nine months ended September 30, 2019, we recorded an approximate non-cash gain of $9.1 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that principally resulted from a lower stock price of $8.40 on September 30, 2019 compared to the stock price of $16.00 on December 31, 2018.

Interest Expense, net (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2020	2019	$	%	2020	2019	$	%
Interest expense, net	$ (419)	$ (467)	$ 48	(10)%	$ (1,083)	$ (1,482)	$ 399	(27)%

Interest expense, net remained flat in the three months ended September 30, 2020 as compared to the three months ended September 30, 2019. Interest expense, net decreased by $0.4 million, or 27%, in the nine months ended September 30, 2020 as compared to the nine months ended September 30, 2019. This decrease was principally due to the decrease in interest expense resulting from the paydown of principal under our 2017 Loan Agreement with Hercules and a lower interest rate that ranged from 9.45% to 9.65% in the nine months ended September 30, 2020 as compared to the interest rate that ranged from 9.70% to 10.2% in the nine months ended September 30, 2019. Principal payments to Hercules resumed during the period from August 1, 2019 through August 1, 2020.

In August 2020, we entered into the 2020 Loan Amendment with Hercules to provide us with the 2020 Loan Facility, an additional term loan in an aggregate principal amount of up to $35.0 million in four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement and for general working capital purposes through the potential commercial launch of FOTIVDA, if approved by the FDA, subject to certain terms and conditions. We received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, including approximately $9.7 million of which was used to retire the outstanding balance under the 2017 Loan Agreement and approximately $5.3 million of which is new loan funding. The 2020 Loan Amendment provides for an initial interest-only period effective for the period from September 1, 2020 through September 1, 2021. See "—Liquidity and Capital Resources—Hercules Loan Facility" below for a description of the 2017 Loan Agreement, 2020 Loan Amendment and 2020 Loan facility.

We anticipate that interest expense will remain flat during the remainder of 2020 and in 2021.

Liquidity and Capital Resources

We have financed our operations to date primarily through private placements and public offerings of our common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. As of September 30, 2020, we had cash, cash equivalents and marketable securities of approximately $68.8 million. See "—Liquidity and Going Concern" below and Note 1 to the condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for a further discussion of our liquidity and the conditions and events which raise substantial doubt regarding our ability to continue as a going concern. Currently, our funds are invested in a U.S. government money market fund and corporate debt securities, including commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below (in thousands):

	Nine Months Ended September 30,	
	2020	2019
Net cash (used in) provided by operating activities	$ (25,103)	$ 4,452
Net cash used in investing activities	(11,152)	—
Net cash provided by financing activities	46,318	28,775
Net increase in cash and cash equivalents	$ 10,063	$ 33,227

Our operating activities used cash of $25.1 million in the nine months ended September 30, 2020 and provided cash of $4.5 million in the nine months ended September 30, 2019. Cash used in operations was principally due to our net income (loss) adjusted for non-cash items and changes in working capital.

Our investing activities used cash of $11.2 million in the nine months ended September 30, 2020 and none in the nine months ended September 30, 2019, principally due to net changes in the maturities and purchases of marketable securities year-to-date as of September 30, 2020. We did not have any marketable securities in the nine months ended September 30, 2019.

Our financing activities provided cash of $46.3 million and $28.9 million in the nine months ended September 30, 2020 and 2019, respectively. In 2020, we raised approximately $52.7 million in funding, including approximately $47.7 million in net proceeds from the sale of approximately 9.7 million shares of our common stock in an underwritten public offering in June 2020 and approximately $5.0 million in new loan funding pursuant to the August 2020 Loan Amendment with Hercules, net of transaction costs. In 2019, we raised approximately $30.3 million in funding, including $7.5 million in net proceeds from the sale of approximately 1.3 million shares of our common stock pursuant to the Leerink Sales Agreement in February 2019, as defined below, and approximately $22.8 million in net proceeds from the sale of approximately 2.2 million shares of our common stock and warrants to purchase an aggregate of 2.5 million shares of our common stock in an underwritten public offering in April 2019. We paid approximately $6.5 million and $1.5 million in principal payments pursuant to our 2017 Loan Agreement with Hercules in the nine months ended September 30, 2020 and 2019, respectively, for which payments had resumed during the period from August 1, 2019 through August 1, 2020.

Public Offering – June 2020

On June 19, 2020, we completed an underwritten public offering of 9,725,000 shares of our common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders each beneficially holding more than 5% of our voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Hercules Loan Facility

On May 28, 2010, we entered into a loan and security agreement with Hercules Capital Inc. and certain of its affiliates, or the First Loan Agreement. The First Loan Agreement was subsequently amended in March 2012, September 2014 and May 2016, or the 2016 Amendment. Amounts borrowed under the amendment in 2012 were repaid in full in 2015.

In December 2017, we refinanced the First Loan Agreement, as amended, by entering into an amended and restated loan and security agreement, or the 2017 Loan Agreement, to refinance our existing loan facility with Hercules and to retire the $20.0 million in secured debt then-outstanding under the First Loan Agreement. Per the terms of the 2017 Loan Agreement, the $20.0 million loan facility had a 42-month maturity from closing, no financial covenants, a lower interest rate and an interest-only period of no less than 12 months, which could be extended up to a maximum of 24 months, assuming the achievement of specified milestones relating to the development of tivozanib.

Pursuant to the 2017 Loan Agreement, the loan maturity date was revised from December 2019 to July 2021. We were not required to make principal payments until February 1, 2019, at which time we would have been required to make 29 equal monthly payments of principal and interest, in the approximate amount of $0.8 million through July 2021. An additional end-of-term payment of approximately $0.8 million is due on July 1, 2021. The financial covenant per the 2016 Amendment to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of our TIVO-3 trial with results that are satisfactory to Hercules was removed. Per the 2017 Loan Agreement, the interest rate decreased from 11.9% to 9.45%.

We must make interest payments on the principal balance of the loan each month it remains outstanding. Per annum interest is payable on the loan balance at the greater of 9.45% and an amount equal to 9.45% plus the prime rate minus 4.75%, as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. In 2018, the interest rate increased to 9.70%, 9.95% and 10.20% in June 2018, September 2018 and December 2018, respectively, due to corresponding increases in the prime rate. In 2019, the interest rate decreased to 9.95%, 9.70% and 9.45% in August 2019, September 2019 and October 2019, respectively, due to corresponding decreases in the prime rate. The interest rate as of August 1, 2020 was 9.45%.

The interest-only period could be extended by two 6-month deferrals of principal payments upon the achievement of specified milestones relating to the development of tivozanib, subject to confirmation by Hercules at its reasonable discretion. In

November 2018, Hercules granted the first 6-month extension of the interest-only period. Accordingly, this resulted in the deferment of principal payments until August 1, 2019, at which time we resumed making 24 equal monthly payments of principal and interest, in the approximate amount of $0.9 million through July 2021. The outstanding principal balance as of August 1, 2020 was approximately $9.7 million.

On August 7, 2020, we entered into the first amendment to the 2017 Loan Agreement, or the 2020 Loan Amendment, to provide us, subject to certain terms and conditions, with the 2020 Loan Facility, an additional term loan in an aggregate principal amount of up to $35.0 million in up to four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement and for general working capital purposes.

We received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, of which approximately $9.7 million was used to retire the outstanding balance under the 2017 Loan Agreement and of which approximately $5.3 million is new loan funding.

The remainder of the loan amount will be available to us subject to certain terms and conditions, including the achievement of the following milestones: (i) the second tranche of $10.0 million would be available through June 30, 2021 assuming FDA approval of FOTIVDA, or Performance Milestone I, (ii) the third tranche, or Tranche Three, of $5.0 million would be available from July 1, 2021 through January 31, 2022 assuming we achieve $20.0 million in net product revenues from sales of FOTIVDA, if approved by the FDA, by no later than December 31, 2021, or Performance Milestone II, and (iii) the fourth tranche of $5.0 million would be available through June 30, 2022 contingent upon the achievement of both Performance Milestone I and Performance Milestone II, and subject to the consent of Hercules.

The 2020 Loan Facility also amends the 2017 Loan Agreement by: (i) extending maturity until September 1, 2023, which is extendable to September 1, 2024 upon our option assuming the Tranche Three funding has occurred, (ii) providing for an interest-only period through September 30, 2021, which is extendable through September 30, 2022 upon the achievement, if at all, of Performance Milestone I, and further extendable through March 31, 2023 after the Tranche Three funding has occurred, if at all, and (iii) revising the per annum interest rate to the greater of (x) 9.65% and (y) an amount equal to 9.65% plus the prime rate as reported in the Wall Street Journal minus 3.25% as determined daily, provided however, that the per annum interest rate shall not exceed 15%. Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of September 30, 2020 was 9.65%.

Per the terms of the 2020 Loan Facility, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. We may prepay all of the outstanding principal and accrued interest under the 2020 Loan Facility, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. We are obligated to make an end-of-term payment of 6.95% of the aggregate amount of loan funding received under the 2020 Loan Facility on the earlier of the maturity of the loan or the date on which we prepay any outstanding loan balance. The approximate $0.8 million end-of-term payment under the 2017 Loan Agreement continues to be due on July 1, 2021. In connection with the 2020 Loan Amendment, we incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The 2020 Loan Facility includes various financial and operating covenants, including that we maintain an unrestricted cash position of at least $10.0 million through the date the Third Tranche funding is received and at least $5.0 million thereafter through the maturity of the loan. We are also required to achieve greater than or equal to 75% of our forecasted net product revenues from our sales of FOTIVDA over a 6-month trailing period, as defined and measured on a monthly basis, effective upon the Third Tranche funding and continuing through the maturity of the loan. The net product revenue covenant will not apply at any time the Third Tranche funding has not been provided nor such advance has been prepaid in full.

The 2020 Loan Facility is secured by substantially all of our assets, excluding intellectual property. The 2020 Loan Facility provides that certain events shall constitute a default by us, including failure by us to pay amounts under the 2020 Loan Amendment when due; breach or default in the performance of any covenant under the 2020 Loan Amendment by us, subject to certain cure periods; our insolvency and certain other bankruptcy proceedings involving us; our default of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon our business.

We have determined that the risk of subjective acceleration under the material adverse events clause included in the 2020 Loan Amendment is remote and, therefore, have classified the outstanding principal amount in current and long-term liabilities based on the timing of scheduled principal payments. As of September 30, 2020, we are in compliance with all of the loan covenants and, through the date of this filing, the lenders have not asserted any events of default under the loan. We do not believe that there has been a material adverse change as defined in the 2020 Loan Amendment.

Public Offering – April 2019

In April 2019, we completed an underwritten public offering of 2,173,913 shares of our common stock and warrants to purchase an aggregate of 2,500,000 shares of our common stock, which we refer to herein as the Offering Warrants, including warrants to purchase an aggregate of 326,086 shares of our common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and will expire two years from the date of issuance. Any Offering Warrants that have not been exercised for cash prior to their expiration shall be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and are separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. As of September 30, 2020, Offering Warrants to purchase 2,500,000 shares of our common stock were outstanding, at an exercise price of $12.50 per share, with an expiration date of April 8, 2021.

Sales Agreement with SVB Leerink

In February 2018, we entered into a sales agreement, or the Leerink Sales Agreement, with SVB Leerink LLC, or SVB Leerink, pursuant to which we may issue and sell shares of our common stock from time to time up to an aggregate amount of $50 million, at our option, through SVB Leerink as our sales agent, with any sales of common stock through SVB Leerink being made by any method that is deemed an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or in other transactions. Any such shares of common stock will be sold pursuant to a prospectus supplement filed under the 2017 Shelf, as defined below. We agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. In the fourth quarter of 2018, we sold approximately 0.5 million shares pursuant to the Leerink Sales Agreement, resulting in approximately $10.3 million in proceeds, net of commissions. In February 2019, we sold approximately 1.3 million shares pursuant to the SVB Leerink Sales Agreement, resulting in proceeds of approximately $7.5 million, net of commissions. As of September 30, 2020, approximately $32.0 million was available for issuance in connection with future stock sales pursuant to the Leerink Sales Agreement.

Universal Shelf Registration Statement

On November 30, 2017, we filed a shelf registration statement on Form S-3 with the SEC, which we refer to as the 2017 Shelf. The 2017 Shelf (File No. 333-221873) was declared effective by the SEC on December 15, 2017 and covers the offering, issuance and sale from time to time of up to $200 million of our common stock, preferred stock, debt securities, warrants and/or units. As of September 30, 2020, approximately $37 million was available for issuance in connection with future stock sales under the shelf registration statement.

Private Placement / PIPE Warrants

In May 2016, we entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which we sold 1,764,242 units, at a price of $9.65 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of our common stock and a PIPE Warrant to purchase one share of our common stock. The PIPE Warrants have an exercise price of $10.00 per share and are exercisable in any manner at any time for a period of five years from the date of issuance. Certain of our directors and executive officers purchased an aggregate of 54,402 units in this offering at the same price as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by us. As of September 30, 2020, PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding, at an exercise price of $10.00 per share, with an expiration date of May 16, 2021.

Liquidity and Going Concern

We have devoted substantially all of our resources to our drug development efforts, comprised of research and development, manufacturing, conducting clinical trials for our product candidates, protecting our intellectual property and general and administrative functions relating to these operations. Our future success is dependent on our ability to develop our product candidates and ultimately upon our ability to attain profitable operations. In March 2020, we submitted an NDA to the FDA for tivozanib as a treatment for relapsed or refractory RCC. In June 2020, the FDA accepted our NDA for substantive review and assigned it a PDUFA target date of March 31, 2021. We anticipate that we will continue to incur significant operating losses for the next several years as we continue our planned development activities for our preclinical and clinical stage assets and commence commercial launch-readiness initiatives in support of a potential commercial launch of tivozanib in RCC. We will require substantial additional funding to continue our planned operating activities, and the timing and nature of activities contemplated for the remainder of 2020 and thereafter will be conducted subject to the availability of sufficient financial resources.

Moreover, we have future payment obligations and cost-sharing arrangements under certain of our collaboration and license agreements. For example, under our agreements with KKC and St. Vincent's, we have royalty obligations with respect to product sales and are required to pay a specified percentage of sublicense revenue in certain instances. In addition, we are required to make certain clinical and regulatory milestone payments under our agreement with St. Vincent's.

During the nine months ended September 30, 2020, we received approximately $58.9 million in funding, including approximately $47.7 million in equity funding from the sale of approximately 9.7 million shares of our common stock in an underwritten public offering in June 2020, approximately $5.0 million in new loan funding pursuant to the August 2020 Loan Amendment with Hercules, net of transaction costs, and approximately $6.2 million in partnership funding for cost sharing obligations, royalties from the sales of FOTIVDA by EUSA and a development milestone payment by KKC.

We believe that our $68.8 million in cash, cash equivalents and marketable securities as of September 30, 2020, along with partnership cost sharing reimbursements, royalty revenues from sales of FOTIVDA by EUSA, product revenues from sales of FOTIVDA, if approved by the FDA, and the additional $20.0 million in available credit under the 2020 Loan Amendment with Hercules, which is available to us subject to achieving the milestones in the 2020 Loan Amendment and described above in "Liquidity and Capital Resources—Hercules Loan Facility" would allow us to fund our planned operations into 2022.

However, under the going concern analysis required by ASC 205-40, the future receipt of potential funding that is contingent on FDA approval of FOTIVDA, such as product revenues from the potential sales of FOTIVDA and the potential future borrowings pursuant to the loan agreement with Hercules, cannot be considered probable at this time because none of our current plans have been finalized at the time of filing this Quarterly Report on Form 10-Q and the implementation of any such plan is not probable of being effectively implemented as none of the plans are entirely within our control. As such, in accordance with the requirements of ASC 205-40, we have determined that we do not have sufficient cash on hand to fund our current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q. This condition raises substantial doubt about our ability to continue as a going concern.

Our plans to address this condition include pursuing one or more of the following options to secure additional funding, none of which can be guaranteed or are entirely within our control:

- Earn royalty payments pursuant to the EUSA Agreement for EUSA's sales of tivozanib in its territory.
- Earn milestone payments pursuant to our collaboration and license agreements or restructure / monetize existing potential milestone and/or royalty payments under those collaboration and license agreements.
- Raise funding through the additional sale of our common stock, including public or private equity financings.
- Drawdown potential future borrowings pursuant to the loan agreement with Hercules, subject to the satisfaction of the conditions to future borrowing.
- Partner a portion or all rights to our portfolio candidates to secure potential additional non-dilutive funds.

Pursuant to our EUSA Agreement, we are entitled to receive up to an additional $4.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France and Italy, and an additional $2.0 million milestone payment for the grant of marketing approval, if any, in three of the licensed countries outside of the EU, as mutually agreed by the parties. These milestone payments are subject to the 30% sublicense fee payable to KKC. We are also eligible to receive additional research and development reimbursement payments from EUSA if EUSA elects to opt-in to the TIVO-3 study. These research and development reimbursement payments would not be subject to the 30% sublicense fee payable to KKC, subject to certain limitations. We may also borrow up to an additional $20.0 million under the 2020 Loan Agreement with Hercules, at our option, contingent upon FDA approval of FOTIVDA and our net product revenue from sales of FOTIVDA, if approved by the FDA, reaching $20.0 million within certain time frames, subject to certain terms and conditions. There can be no assurance, however, that the FDA will approve FOTIVDA or that the other conditions to the funding of such loan amounts will be satisfied.

There can be no assurance that we will receive cash proceeds from any of these potential resources or to the extent cash proceeds are received such proceeds would be sufficient to support our current operating plan for more than the next twelve months from the date of filing this Quarterly Report on Form 10-Q. Refer to"— Risk Factors. *We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern*," included elsewhere in this Quarterly Report on Form 10-Q.

There are numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products. Accordingly, our future funding requirements may vary from our current expectations and will depend on many factors, including, but not limited to:

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of researching and developing our product candidates, and of conducting preclinical and clinical trials;
- the timing of, and the costs involved in, completing our clinical trials and obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our 2017 Loan Agreement or 2020 Loan Amendment with Hercules or under any other agreements with third parties;
- the cost and outcome of any legal actions against us, including the current lawsuits described under the heading "Part II, Item 1 – Legal Proceedings";
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;
- the timing, receipt and amount of sales of, or royalties on, FOTIVDA and our future products, if any;
- general economic, industry and market conditions;
- the impact of COVID-19 on our operations, business and prospects; and
- our ability to continue as a going concern.

We will require additional funding to extend our planned operations. We may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all. If we are unable to raise substantial additional capital in the near term, whether on terms that are acceptable to us, or at all or if we were to default under the 2017 Loan Agreement or 2020 Loan Amendment with Hercules, and Hercules accelerated the then remaining principal payments and fees due under the loan, then we may be required to:

- delay, limit, reduce or terminate our clinical trials or other development activities for one or more of our product candidates; and/or
- delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, if approved.

Contractual Obligations and Commitments

There have been no additional material changes to our contractual obligations and commitments outside the ordinary course of business from those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2019 filed with the SEC on March 16, 2020, except as discussed below.

On March 5, 2020, we entered into a sublease agreement for office space located at 30 Winter Street in Boston, Massachusetts (the “Winter Street Sublease”) to relocate our corporate headquarters located at One Broadway in Cambridge, Massachusetts. Under the terms of the Winter Street Sublease, we lease 10,158 square feet of office space for $47.00 per square foot, or approximately $0.5 million per year in base rent subject to certain operating expenses, taxes and annual base rent increases of approximately 3%. The sublease term will continue through November 29, 2022.

In March 2020, we decided to discontinue the CyFi-2 trial, which is a randomized phase 2 clinical trial evaluating ficlatuzumab in combination with high-dose cytarabine versus high-dose cytarabine alone in patients with AML that we initiated in November 2019, due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which has impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial drug supply.

On August 7, 2020, we entered into the 2020 Loan Amendment with Hercules to provide us with the 2020 Loan Facility, an additional term loan of up to $35.0 million in four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement and for general working capital purposes through the potential commercial launch of FOTIVDA, if approved by the FDA, subject to certain terms and conditions, as described above in "Liquidity and Capital Resources—Hercules Loan Facilty."

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Item 4. Controls and Procedures.

Our management, with the participation of our President and Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of September 30, 2020. The term "disclosure controls and procedures" means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our President and Chief Executive Officer and Chief Financial Officer concluded that as of September 30, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, during the quarter ended September 30, 2020 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

On July 24, 2020, the District Court for the District of Massachusetts dismissed a purported class action filed against us in 2019. This purported class action lawsuit, which we refer to as the 2019 Class Action, was filed against us and certain of our present and former officers, Michael Bailey, Matthew Dallas, and Keith Ehrlich, on February 25, 2019, in the Southern District of New York for the District of New York, captioned *David Hackel v. AVEO Pharmaceuticals, Inc., et al*, No. 1:19-cv-01722-AT. On April 12, 2019, the court granted the defendants' motion to transfer the action to the District of Massachusetts (Case No. 1:19-cv-10783-JCB). On May 6, 2019, the court appointed Andrej Hornak as lead plaintiff and approved Pomerantz LLP as lead counsel and Andrews DeValerio LLP as liaison counsel. On July 24, 2019, the plaintiffs filed an amended complaint naming Michael Needle as an additional defendant. The amended complaint purported to be brought on behalf of shareholders who purchased our common stock between May 4, 2017 through January 31, 2019. It generally alleged that we and our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by failing to disclose and/or making allegedly false and/or misleading statements about the estimated dates by which we would report the topline results from the TIVO-3 trial, the preliminary overall survival results from the TIVO-3 trial, the sufficiency of the overall survival data from the TIVO-3 trial, the timing of the NDA submission, and the risk of FDA approval. The complaint sought unspecified damages, interest, attorneys' fees, and other costs. On September 27, 2019, we filed a motion to dismiss the amended complaint. On July 24, 2020, the District Court granted our motion to dismiss. The time for appeal expired in August 2020 without appeal.

In connection with the filing of the 2019 Class Action, two derivative lawsuits were filed on July 8, 2019 and July 10, 2019 against us, certain of our present and former officers and our directors in the Suffolk Superior Court, Commonwealth of Massachusetts, captioned *Stephen Favre v. Michael P. Bailey, et al*. 19-2169-BLS2 and *Jianbin Yu v. Michael P. Bailey, et al.* 19-2188-BLS2, respectively. The complaints generally allege breach of fiduciary duty, unjust enrichment, and waste of corporate assets due to the 2019 Class Action and the actions alleged therein. On July 26, 2019, the court granted the parties' joint motion to consolidate the cases and stay the consolidated matter pending the dismissal of, or filing of an answer to, the complaint in the 2019 Class Action. Given the dismissal of the 2019 Class Action in July 2020, the derivative plaintiffs have agreed to dismiss the derivative lawsuit without prejudice. We anticipate a stipulation will be filed with the court soon.

Item 1A. Risk Factors

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Quarterly Report on Form 10-Q and other filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Quarterly Report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC. These risk factors restate and supersede the risk factors set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2019.

Risks Related to the COVID-19 Pandemic

The COVID-19 pandemic has adversely disrupted, and is expected to continue to adversely disrupt our operations, including our ability to complete our ongoing clinical trials and may have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

We have enrolled and seek to enroll cancer patients in our ongoing clinical trials at sites located both in the United States and in Europe. The COVID-19 pandemic has delayed and may continue to delay or otherwise adversely affect these clinical development activities, including our ability to recruit and retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, availability of hospital staff supporting the conduct of our clinical trials, and the reluctance of patients enrolled in our clinical trials to visit clinical trial sites;
- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples, and other supplies used in our clinical trials;
- the impact of further limitations on travel that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites, or the ability of employees at any of our contract manufacturers or contract research organizations to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials, and limit the amount of clinical data we will be able to report;
- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations or, in the case of combination trials, our study collaborators, due to staffing shortages, production slowdowns or stoppages, or disruptions in delivery systems; and
- availability of future capacity at contract manufacturers to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products.

For example, some of the clinical trial sites for our DEDUCTIVE trial have suspended enrollment at times due to COVID-19 related hospital and governmental restrictions. Enrollment has occurred at a slower pace than initially forecasted prior to the onset of the pandemic, and we cannot guarantee the future pace of enrollment. In addition, in-person monitoring visits are currently on hold at certain of the clinical trial sites in our DEDUCTIVE trial and to the extent possible due to the COVID-19 pandemic, monitoring is being conducted remotely. We do not yet know whether remote management of this function will prove to be sufficient. The extent of any adverse impact on our clinical trials will depend on numerous evolving factors that cannot be predicted with any level of certainty. In addition, in March 2020 we decided to discontinue the CyFi-2 trial due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the ficlatuzumab clinical trial supply.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results. In addition, our clinical trial patients who contract COVID-19 may have adverse health outcomes unrelated to their cancer that could impact the results of our clinical trials.

In light of the COVID-19 pandemic, we are designing our strategic commercial approach for tivozanib to be flexible by building remote as well as in-person customer engagement capabilities in preparation for potential commercialization. However, it is uncertain whether obstacles and changes to standard sales and marketing practices resulting from the COVID-19 pandemic, including the shift from in-person to telephonic and virtual interactions with healthcare professionals, could negatively impact our commercialization efforts.

The COVID-19 pandemic continues to rapidly evolve and its ultimate scope, duration and effects are unknown. The extent of the impact of the disruptions to our business, preclinical studies, clinical trials and commercialization efforts as a result of the outbreak will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could adversely impact our ability to raise additional funds through public offerings or private placements and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations, and prospects.

Risks Related to Our Financial Position and Need for Additional Capital

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We may be forced to delay or reduce the scope of our development programs and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

As September 30, 2020, we had approximately $68.8 million in cash, cash equivalents and marketable securities. On August 7, 2020, we entered into the 2020 Loan Amendment with Hercules. The 2020 Loan Amendment provides us with the 2020 Loan Facility that includes up to $20.0 million in additional loan funding contingent upon FDA approval of FOTIVDA and our net product revenues from sales of FOTIVDA, if approved by the FDA, within certain time frames and subject to certain terms and conditions.

However, under the going concern analysis required by ASC 205-40, the future receipt of cash flows that are contingent on FDA approval of FOTIVDA, such as product revenues from the potential sales of FOTIVDA and the potential future borrowings pursuant to the loan agreement with Hercules, cannot be considered probable at this time because none of our current plans have been finalized at the time of filing this Quarterly Report on Form 10-Q and the implementation of any such plan is not probable of being effectively implemented as none of the plans are entirely within our control. As such, in accordance with the requirements of ASC 205-40, we have determined that we do not have sufficient cash on hand to fund our current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q. This condition raises substantial doubt about our ability to continue as a going concern within one year after the date the financial statements included elsewhere in this Quarterly Report on Form 10-Q are issued. Management's plans in this regard are described in Note 1 of the condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q. We cannot guarantee that we will receive cash proceeds from any of these potential resources or to the extent cash proceeds are received such proceeds would be sufficient to support our current operating plan for more than the next twelve months from the date of filing this Quarterly Report on Form 10-Q. In addition, we cannot guarantee that we will be able to obtain sufficient additional funding when needed or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that these plans cannot be effectively realized, there can be no assurance that we will be able to continue as a going concern.

We have incurred significant operating losses since inception and anticipate that we will continue to incur significant operating losses for the foreseeable future. It is uncertain if we will ever attain profitability.

We have a history of incurring operating losses and as of September 30, 2020, we had an accumulated deficit of $609.7 million. To date, we have not commercialized any products or generated any material revenues from the sale of products. Absent the realization of sufficient revenues from product sales, we may never attain profitability. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that we will continue to incur significant operating costs over the next several years as we seek to develop and commercialize our product candidates. As noted above, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

If we do not successfully develop and obtain and maintain regulatory approval for our existing and future pipeline of product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales. Even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We will require substantial additional funding, and a failure to obtain this necessary capital when needed would force us to delay, limit, reduce or terminate our research, product development or commercialization efforts.

We will require substantial additional funds to continue our development programs and to fulfill our planned operating goals. In particular, our currently planned operating and capital requirements include the need for substantial working capital to support development and commercialization activities for tivozanib. Moreover, we have future payment obligations and cost-sharing arrangements under certain of our collaboration and license agreements. For example, under our agreements with KKC and St. Vincent's, we have royalty obligations with respect to product sales and are required to pay a specified percentage of sublicense revenue in certain instances. In addition, we are required to make certain clinical and regulatory milestone payments under our agreement with St. Vincent's.

We believe that our $68.8 million in cash, cash equivalents and marketable securities as of September 30, 2020, along with partnership cost sharing reimbursements, royalty revenues from sales of FOTIVDA by EUSA, product revenues from sales of FOTIVDA, if approved by the FDA, and the additional $20.0 million in available credit under the 2020 Loan Amendment with Hercules, which is available to us subject to achieving the milestones in the 2020 Loan Amendment and described above in "Liquidity and Capital Resources—Hercules Loan Facility" would allow us to fund our planned operations into 2022.

However, prior to generating product revenues from the potential commercialization of FOTIVDA, if approved by the FDA, and the $20.0 million in potential future borrowings pursuant to the loan agreement with Hercules that is contingent upon FDA approval of FOTIVDA and our product revenues from potential sales of FOTIVDA, subject to certain terms and conditions, we do not have sufficient cash on hand to fund our current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q. See "—We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern." Accordingly, the timing and nature of activities contemplated for the remainder of 2020 and thereafter will be conducted subject to the availability of sufficient financial resources.

Furthermore, there are numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products. Accordingly, our future capital requirements may vary from our current expectations and depend on many factors, including but not limited to:

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of researching and developing our product candidates and of conducting preclinical and clinical trials;
- the timing of, and the costs involved in, completing our clinical trials and obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our 2017 Loan Agreement or 2020 Loan Amendment with Hercules, or under any other agreements with third parties;
- the cost and outcome of any legal actions against us, including the current lawsuits described above under the heading "Part II, Item 1 – Legal Proceedings";
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;
- the timing, receipt and amount of sales of, or royalties on, FOTIVDA and our future products, if any;
- general economic, industry and market conditions,
- the impact of COVID-19 on our operations, business and prospects; and
- our ability to continue as a going concern.

We will require additional funding to extend our planned operations. We may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. For example, we may never achieve the milestones specified in the 2020 Loan Amendment with Hercules that would allow us to access the remaining $20.0 million in available credit. We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all.

If we are unable to raise substantial additional capital in the near term, whether on terms that are acceptable to us, or at all, or we were to default under the 2017 Loan Agreement or 2020 Loan Amendment with Hercules and Hercules accelerates the then remaining principal payments and fees due under the loan, then we may be required to:

- delay, limit, reduce or terminate our clinical trials or other development activities for one or more of our product candidates; and/or
- delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, if approved.

Failure to comply with the covenants or payment obligations under the 2017 Loan Agreement or the 2020 Loan Amendment could result in an event of default, which could materially and adversely affect our business and our financial condition.

The 2017 Loan Agreement and 2020 Loan Amendment include certain financial and operational covenants and provide for certain occurrences that constitute events of default. Certain of those covenants may be out of our control, such as failure to achieve net product revenue at a certain percentage of projected net product revenue. Potential events of default also include circumstances occurring that have a material adverse effect on our business, our insolvency or bankruptcy, or default on our other obligations or agreements. If we fail to make payments when due, breach any operational covenant or have any event of default, Hercules could require us to immediately repay all outstanding principal and accrued interest on the loan, plus a prepayment charge, which could have a material adverse effect on our business and financial condition

We are a development stage company, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Other than the European and the New Zealand marketing approvals for tivozanib (FOTIVDA) received by our partner EUSA in August 2017 and July 2019, respectively, all of our product candidates are in the development stage. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. Preclinical studies and clinical trials may involve highly uncertain results and a high risk of failure.

Moreover, positive data from preclinical studies and clinical trials of our product candidates may not be predictive of results in ongoing or subsequent preclinical studies and clinical trials and may not demonstrate the results necessary to support the filing of an NDA with the FDA or to obtain marketing approval in a particular market. For example, although we announced positive topline results for the primary endpoint of the TIVO-3 trial in November 2018, in January 2019, the FDA recommended that we not submit an NDA for tivozanib at that time as the first interim OS results from the TIVO-3 trial did not allay its concerns about a potential detriment in OS from the TIVO-1 trial. In August 2019, we performed a second prespecified interim OS analysis, which showed an updated OS hazard ratio of 0.99 (p=0.95), estimating that tivozanib resulted in a 1% lower risk of death for patients in the trial relative to sorafenib. In May 2020, we performed a final OS analysis, which showed a final OS hazard ratio of 0.97 (p=0.82). In June 2020, the FDA accepted our tivozanib NDA for substantive review and assigned it a PDUFA target date of March 31, 2021. Although the final OS analysis yielded an OS hazard ratio below 1.00 and was similar to those observed with prior FDA-approved VEGFR TKI vs. VEGFR TKI pivotal studies in RCC, if the FDA does not find that the results of the tivozanib clinical trials adequately demonstrate a favorable risk-benefit profile for tivozanib in RCC, we may not be able to obtain marketing approval from the FDA to commercialize tivozanib in the United States.

Any NDA we submit to the FDA may not be approved by the FDA and even if approved, we may not be able to successfully commercialize products in the United States. Moreover, any IND we submit to commence a clinical trial may not be accepted for filing. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had more experience developing and commercializing our product candidates.

In addition, as a development stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks Related to Development and Commercialization of Our Drug Candidates

In the near term, we are substantially dependent on the success of tivozanib. If we are unable to complete the clinical development of, obtain and maintain marketing approval for or successfully commercialize tivozanib, either alone or with our collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

Other than the marketing approvals for tivozanib (FOTIVDA) received by our partner EUSA, we currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of tivozanib for marketing approval in North America. Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize tivozanib in North America in one or more disease indications.

The success of tivozanib will depend on a number of factors, including the following:

- our ability to secure the substantial additional capital required to complete clinical trials of tivozanib, including the DEDUCTIVE trial, and to fund the activities necessary to successfully commercially launch tivozanib if it receives regulatory approval for marketing in the United States;
- successful design, enrollment and completion of clinical trials;
- a safety, tolerability and efficacy profile that is satisfactory to the FDA, EMA or any other comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities such as the FDA;
- the performance of the contract research organizations, or CROs, we have hired to manage our clinical studies, as well as that of our collaborators and other third-party contractors;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- maintenance of existing or establishment of new supply arrangements with third-party raw materials suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for tivozanib and finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with KKC;
- protection of our rights in our intellectual property portfolio, including our ability to maintain our license agreement with KKC;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors;
- successful identification of biomarkers for patient selection; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical trial results, the availability of adequate capital, the regulatory approval process, potential threats to our intellectual property rights and the development, manufacturing, marketing and sales efforts of our collaborators. If we are unable to develop, receive marketing approval for and successfully commercialize tivozanib on our own or with our collaborators, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of tivozanib is our primary focus, as part of our growth strategy, we are developing a pipeline of product candidates. These other product candidates will require additional, time-consuming and costly development efforts, by us or by our collaborators, prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace, or will be more effective than other commercially available alternatives.

Results of early clinical trials may not be predictive of results of later clinical trials, and interim results of clinical trials may not be predictive of the final results or the success of clinical trials.

The outcome of early clinical trials, such as our phase 1b/2 TiNivo trial, our phase 1b/2 DEDUCTIVE trial and our ficlatuzumab trials in HNSCC, AML and pancreatic cancer, may not be predictive of the success of later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we have, and could in the future, face similar setbacks. In addition, interim results and analyses of clinical trials do not necessarily predict the final results or the success of a trial once it is complete.

While the design of a clinical trial may help to establish whether its results will support approval of a product, flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates. For example, in June 2013, the FDA issued a complete response letter, or the 2013 CRL, informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS. Our current TIVO-3 clinical trial was designed to address the FDA's concerns about the negative OS trend expressed in the 2013 CRL. If the FDA does not find that the results of the TIVO-3 trial, together with the results of our prior tivozanib clinical trials, adequately demonstrate a favorable risk-benefit profile for tivozanib in RCC we may not be able to obtain marketing approval from the FDA to commercialize tivozanib in the United States.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

If preclinical or clinical trials of any product candidates that we or our collaborators may develop fail to demonstrate satisfactory safety and efficacy to the FDA and other regulators, we or our collaborators may incur additional costs or delays or may be unable to complete the development and commercialization of these product candidates.

We and any collaborators, including our partners and sublicensees, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. We and our collaborators must complete extensive preclinical development and clinical trials that demonstrate the safety and efficacy of our product candidates in humans before we can obtain these approvals.

Preclinical and clinical testing is expensive, is difficult to design and implement, and can take many years to complete. It is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, as well as failure to demonstrate efficacy at all in a clinical trial or across a broad population of patients, the occurrence of adverse events that are medically severe or commercially unacceptable, failure to comply with protocols or regulatory requirements and determination by the applicable regulatory authority that a product candidate may not continue development or is not approvable. Even if a product candidate has a beneficial effect, that effect may not be detected during preclinical or clinical evaluation due to a variety of factors, including the size, duration, design, measurements, conduct or analysis of our preclinical and clinical trials. Conversely, as a result of the same factors, our preclinical or clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our preclinical or clinical trials we may fail to detect toxicity or intolerability of our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to timely or successfully complete preclinical and clinical development and demonstrate the results necessary to support regulatory approvals could result in additional unplanned costs and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond those planned, or if the results of these trials or tests are unfavorable, uncertain, only modestly favorable or indicate safety concerns, we or our collaborators, may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval would significantly harm our business.

Adverse events, undesirable side effects or other unexpected properties of our product candidates may be identified during development that could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib, ficlatuzumab or our other product candidates could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt preclinical or clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound.

If we or our collaborators experience any of a number of possible complications in connection with preclinical or clinical trials of our product candidates, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We or our collaborators may experience numerous complications in connection with preclinical or clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our product candidates including:

- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delay or failure to reach agreement on clinical trial contracts or clinical trial protocols with prospective trial sites;
- unfavorable or inconclusive clinical trial results;

- our decision or a regulatory recommendation or order to conduct additional clinical trials or abandon product development programs;
- the number of patients required for our clinical trials may be larger than anticipated, patient enrollment may be slower than anticipated or participants may drop out of these clinical trials at a higher rate than anticipated;
- the costs of our clinical trials may be greater than we anticipate;
- our third-party contractors, including those manufacturing our product candidates, or conducting clinical trials on our behalf, may fail to successfully comply with regulatory requirements or meet their contractual obligations in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to increase the needed enrollment size for the clinical trial, extend the clinical trial's duration, or drop the patients from the final efficacy analysis for the clinical trial, which can negatively affect the statistical power of the results;
- our decision, or a decision by regulators or institutional review boards, that may require us to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' clinical trial designs or interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Further, the COVID-19 pandemic has impacted and we expect that it will continue to impact our clinical trials as described above in "Risks Related to the COVID-19 Pandemic."

Product development costs for us and our collaborators will increase if we experience delays in testing or pursuing marketing approvals, and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization. We do not know whether any trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;

- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment; and
- competing clinical trials.

In addition, participation in our clinical trials will be affected by clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied and the drug being provided as a control in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. For example, at the request of the FDA, we have updated the forms used to obtain consent from patients in ongoing and future trials with tivozanib to include information about the OS results from the TIVO-3 trial as well as the other tivozanib clinical trial OS results to date. These results may impact the interest of clinicians and patients in participating in future clinical trials with tivozanib.

Further, the COVID-19 pandemic has impacted and we expect that it will continue to impact our clinical trials as described above in "Risks Related to the COVID-19 Pandemic."

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to commence sales of and generate revenues from our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

We are conducting, and intend in the future to conduct, clinical trials for certain of our product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We are conducting, and intend in the future to conduct, one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

We may not obtain marketing approvals for our product candidates.

We may not obtain marketing approval for our product candidates. It is possible that the FDA or comparable foreign regulatory agencies may refuse to accept for substantive review any future application that we or a collaborator may submit to market and sell our product candidates, or that any such agency may conclude after review of our or our collaborator's data that such application is insufficient to obtain marketing approval of our product candidate.

In June 2013, for example, the FDA issued the 2013 CRL informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS. Our TIVO-3 clinical trial was designed to address the FDA's concerns about the negative OS trend expressed in the 2013 CRL. If the FDA does not find the results of TIVO-3 and our other tivozanib clinical trials to adequately demonstrate a favorable risk-benefit profile for tivozanib in RCC, then the FDA may not grant marketing approval for tivozanib.

If the FDA or other comparable foreign regulatory agency does not accept or approve our NDA for tivozanib or any application to market and sell any of our product candidates, such regulators may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before they will reconsider our application. Depending on the extent of these or any other required trials or studies, approval of any application that we submit may be delayed by several years, or may require us or our collaborator to expend more resources than we or they have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or other foreign regulatory agency to approve our applications for marketing and commercialization.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us or our collaborators from commercializing our product candidates and generating revenues. If any of these outcomes occur, we would not be eligible for certain milestone and royalty revenue under our partnership agreements, our collaborators could terminate our partnership agreements, and we may be forced to abandon our development efforts for our product candidates, any of which could significantly harm our business.

Even if a product candidate receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the product, and could cause regulatory authorities to take certain regulatory actions.

Clinical trials of our product candidates will be conducted in carefully defined subsets of patients who have agreed to participate. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any of our collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we, or any of our collaborators, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any of our collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- physicians and patients may stop using our product; and
- our reputation may suffer.

Any of these events could harm our business and operations and could negatively impact our stock price.

In August 2017, the European Commission granted marketing authorization to EUSA for tivozanib in Europe. In January 2019, the EMA's Committee for Medicinal Products for Human Use, or CHMP, requested the topline data results from our TIVO-3 trial for review under its post-authorization monitoring procedures. Subsequently, EUSA has informed us that the CHMP has requested additional data updates and analysis from our TIVO-3 trial, including the final OS analysis received in May 2020. If the EMA finds that the results from the TIVO-3 trial raise questions on the safety or efficacy of FOTIVDA and the risk-benefit assessment on which the marketing authorization for FOTIVDA in the EU was based, the EMA could take certain post-authorization measures with regards to FOTIVDA such as requiring EUSA to conduct additional post-authorization studies, or risk management measures as part of an extended pharmacovigilance monitoring, or a change of the labeling and use instructions for FOTIVDA. If its concerns would not be addressed by other post-authorization measures, the EMA or the European Commission could also determine to change, suspend or revoke the previously granted marketing authorization for FOTIVDA. Any such actions taken by the European regulatory authorities with respect to the marketing authorization for FOTIVDA could have a material adverse effect on our ability to receive milestone, royalty or other payments from EUSA related to the approval and/or sales of FOTIVDA and on our business, operations and prospects.

Even if our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. There are already a number of therapies on the market competitive to tivozanib, as well as our other product candidates, in indications we intend to target.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. In light of the COVID-19 pandemic, we are designing our strategic commercial approach for tivozanib to be flexible by building remote as well as in-person customer engagement capabilities in preparation for potential commercialization. However, it is uncertain whether obstacles and changes to standard sales and marketing practices resulting from the COVID-19 pandemic, including the shift from in-person to telephonic and virtual interactions with healthcare professionals, could negatively impact our commercialization efforts.

If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the advantages of the product compared to competitive therapies;
- the number of competitors approved for similar uses;
- the relative promotional effort of us as compared with our competitors;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;

- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- the timing of market introduction of our approved products as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of their potential for marketing approval and commercialization, as well as those that are most aligned with our strategic goals. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have sales, marketing or distribution infrastructure and have limited experience as an organization in the sales, marketing, and distribution of pharmaceutical products. Our licensee EUSA has been responsible for the sales, marketing, and distribution efforts associated with the commercial launch of tivozanib in certain European countries. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and, if not initiated sufficiently in advance of marketing approval, could delay any product launch. Conversely, if the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could incur substantial costs and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

If we enter into arrangements with third parties to perform sales, marketing and distribution services such as our collaboration with EUSA, our product revenues or the profitability of these products may be substantially lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

We may seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

If we are unable to successfully develop companion diagnostics for certain of our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of these therapeutics.

A component of our business strategy may be to develop, in collaboration with a third party, companion diagnostics for some of our therapeutic product candidates. There has been limited success to date industry-wide in developing companion diagnostics. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have limited experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates. The FDA and similar regulatory authorities outside the United States are generally expected to regulate companion diagnostics as medical devices. In each case, companion diagnostics require separate regulatory approval prior to commercialization. We expect to rely in part on third parties for the design, development and manufacture of any companion diagnostic. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so, the development of our therapeutic product candidates may be adversely affected, our therapeutic product candidates may not receive marketing approval and we may not realize the full commercial potential of any therapeutics that receive marketing approval. As a result, our business would be harmed, possibly materially.

We face substantial competition from existing approved products. Our competitors may also discover, develop or commercialize new competing products before, or more successfully, than we do.

The biotechnology and pharmaceutical industries are highly competitive, and our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of product candidates. Our corporate objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect any product candidate that we commercialize either independently or with our strategic partners will compete with existing, market-leading products.

There are many companies focused on the development of small molecules and antibodies for cancer treatment. Our core competitors include pharmaceutical and biotech organizations, as well as academic research institutions, clinical research laboratories and government agencies that are pursuing research activities in the same therapeutic area. Many of our competitors have greater financial, technical and human resources than we do. Additionally, many competitors have greater experience in product discovery and development, obtaining FDA and other regulatory approvals, and commercialization capabilities, which may provide them with a competitive advantage.

We believe that our ability to compete will depend on our ability to execute on the following objectives:

- design, develop and commercialize products that are superior to other products in the market in terms of, among other things, safety, efficacy, convenience, or price;
- obtain patent and/or other proprietary protection for our processes and product candidates;
- obtain required regulatory approvals;
- obtain favorable reimbursement, formulary and guideline status; and
- collaborate with others in the design, development and commercialization of our products.

Established competitors may invest heavily to discover and develop novel compounds that could make our product candidates obsolete. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to obtain approval, to overcome price competition and to be commercially successful. If we are not able to compete effectively, our business will not grow and our financial condition and operations will suffer.

The competitive landscape and treatment regimens for RCC and HCC continue to rapidly evolve, particularly given the entrance of immune checkpoint inhibitor combination therapies and the potential entrance of immune checkpoint inhibitor and VEGFR TKI combination therapies into the RCC treatment landscape. The utilization of such regimens may affect sequencing of certain drugs and combinations across different lines of therapy. Additionally, there are several therapies in clinical development for RCC and HCC that may alter the competitive landscape for the treatment of these cancers. As such, it is difficult to predict how these changes will inform our perspective on the key competitors of tivozanib in RCC and HCC in the future.

We believe the key competitors for tivozanib in relapsed or refractory RCC include the following FDA-approved treatments: Exelixis' Cabometyx (cabozantinib), Novartis' Afinitor (everolimus), Pfizer's Inlyta (axitinib), BMS's Opdivo (nivolumab), and Bayer's Nexavar (sorafenib), all as single-agent therapies; along with the combination of Eisai's Lenvima (lenvatinib) and Novartis' Afinitor (everolimus). In addition, other FDA-approved treatments for advanced RCC in the first line and/or subsequent lines of therapy include the combinations of Merck's Keytruda (pembrolizumab) and Pfizer's Inlyta (axitinib), BMS's Yervoy (ipilimumab) and Opdivo (nivolumab), and Pfizer's Inlyta (axitinib) and Merck KGaA's Bavencio (avelumab); as well as the single agents of Pfizer's Sutent (sunitinib), Pfizer's Torisel (temsirolimus), and Novartis' Votrient (pazopanib). Additionally, there are a number of therapies in development for RCC, including Merck's MK-6482 as a single agent, the combination of Calithera Biosciences's CB-938 and Exelixis' Cabotmetyx (cabozantinib), the combination of BMS's Opdivo (nivolumab) and Exelixis' Cabotmetyx (cabozantinib), the combination of Eisai's Lenvima (lenvatinib) and Merck's MK-6482, and the combination of Roche's Tecentriq (atezolizumab) and Exelixis' Cabometyx (cabozantinib).

We believe the key competitors for tivozanib in advanced HCC include the following FDA-approved treatments: Roche's Tecentriq (atezolizumab) and Avastin (bevacizumab) in combination and BMS's Yervoy (ipilimumab) and Opdivo (nivolumab) in combination; as well as Bayer's Nexavar (sorafenib); Bayer's Stivarga (regorafenib); Eisai's Lenvima (lenatinib); Exelixis' Cabometyx (cabozantinib); Eli Lilly's Cyramza (ramucirumab); BMS's Opdivo (nivolumab); and Merck's Keytruda (pembrolizumab), all as single agents. Additionally, there are a number of therapies in clinical development for advanced HCC and it is difficult to predict which will be the key competitors to tivozanib in this indication.

We believe the products that are considered competitive with ficlatuzumab include those agents exclusively targeting the HGF/c-Met pathway. We believe the most direct competitors to our AV-203 program are monoclonal antibodies that specifically target the ErbB3 receptor. With respect to AV-380, Megace is the only approved agent for the treatment of cachexia. A number of agents with unique mechanisms of action are in various stages of clinical development in cachexia or muscle wasting. We believe the key competitors for our AV-380 program are other companies pursuing the GDF-15 pathway for cachexia, including NGM Biopharmaceuticals Inc. and Pfizer. In connection with AV-353, we are not aware of any ongoing clinical trials of Notch 3-specific inhibitors or any approved Notch 3-specific inhibitors in oncology; however, a number of agents for applications in oncology are being explored which target the Notch 3 receptor and may inhibit other Notch receptors.

Even if we or our collaborators are able to commercialize any product candidate, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health care programs and private health insurers. For example, our European licensee for tivozanib, EUSA, is currently in the process of seeking reimbursement approval for tivozanib in many of the countries in which tivozanib has been approved. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us or our collaborators to establish or maintain pricing sufficient to realize a sufficient return on our investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often time consuming and costly and may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any collaborators, to commercialize successfully any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably. These payors may not view our products, even if approved, as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products to be marketed on a competitive basis. Cost-control initiatives could cause us or our collaborators to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, for example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense could require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for our product candidates;
- withdrawal of clinical trial participants;
- delay or termination of our clinical trial;
- significant costs to defend the related litigation;
- diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize our product candidates;
- injury to our reputation and negative media attention; and
- a decline in our stock price.

Our inability to maintain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical studies in the amount of $20 million in the aggregate. We will need to increase our insurance coverage if we commercialize any product that receives marketing approval. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. The cost of any such product liability litigation or other proceeding, even if resolved in our favor, could be substantial. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as CROs, to conduct clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We, in consultation with our collaborators, where applicable, design the clinical trials for our product candidates, but we rely on CROs and other third parties to perform many of the functions in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties. In addition, these third parties may be adversely affected by the COVID-19 pandemic.

Although we plan to continue to rely on these third parties to conduct our ongoing and any future clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, including good clinical practices, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. The third parties on whom we rely generally may terminate their engagements with us at any time. If we are required to enter into alternative arrangements because of any such termination, the introduction of our product candidates to market could be delayed.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain, process and analyze is compromised for any reason, including their failure to adhere to our clinical trial protocols or regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may experience delays or may fail to meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates and our reputation could be harmed.

We rely on third-party manufacturers to produce our preclinical and clinical product candidate supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates. Any failure by a third-party manufacturer to produce supplies for us may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We do not possess all of the capabilities to fully commercialize any of our product candidates on our own. We have relied upon third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future. If we are unable to arrange for third-party manufacturing sources, or to do so on commercially reasonable terms, we may not be able to complete development of such product candidates or to market them.

Reliance on third-party manufacturers entails certain risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications), failure of the third party to accept orders for supply of drug substance or drug product and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. Other risks of our reliance on third-party manufacturers include the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified; the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and the possible misappropriation of our proprietary information, including our trade secrets and know-how. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to current good manufacturing practices, or current good manufacturing practices, or cGMPs. Any failure by our third-party manufacturers to comply with cGMP or failure to scale-up manufacturing processes as needed, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for action by the FDA to withdraw approvals for product candidates previously granted to us and for other regulatory action, including recall or seizure, fines, imposition of operating restrictions, total or partial suspension of production or injunctions.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies and potential commercial manufacturing. There are a small number of suppliers of raw and starting materials that we use to manufacture our product candidates. Such suppliers may not sell these materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. In addition, other factors that are hard to predict or beyond our or our manufacturers' control, such as natural disasters, fires or explosions, political unrest, terrorism, generalized labor unrest, or health pandemics could damage or disrupt our manufacturers' operations.

Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial or potential commercial launch due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our supply chain is disrupted due to any of these factors after regulatory approval has been obtained for our product candidates, there could be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Because of the complex nature of many of our early stage compounds and product candidates, our manufacturers may not be able to manufacture such compounds and product candidates at a cost or quantity or in the timeframe necessary to develop and commercialize the related products. If we successfully commercialize any of our drugs, we may be required to establish or access large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline matures, we will have a greater need for commercial manufacturing capacity. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing in the event that one or more of our product candidates gains marketing approval, third parties with whom we currently work may need to increase their scale of production or we may need to secure alternate suppliers.

We may not be successful in establishing or maintaining strategic partnerships to further the development of our therapeutic programs. Additionally, if any of our current or future strategic partners fails to perform its obligations or terminates the partnership, the development and commercialization of the product candidates under such agreement could be delayed or terminated. Such failures could have a material adverse effect on our operations and business.

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships with major biotechnology or pharmaceutical companies to support the development and commercialization of our product candidates. In these partnerships, we would expect our strategic partner to provide capabilities in research, development, marketing and sales, in addition to funding.

We face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any product candidates and programs because our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential.

If we are not able to establish and maintain strategic partnerships:

- the development of certain of our product candidates may be delayed or terminated;
- the internal cash expenditures needed to develop such product candidates would increase significantly, and we may not have the cash resources to develop such product candidates on our own; and
- we may have fewer resources with which to continue to operate our business.

Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us. Furthermore, we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed, sales of an approved product are disappointing or the partner experiences its own financial or operational constraints or a change in business strategy. If any current or future strategic partners do not devote sufficient time and resources to their arrangements with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be adversely affected. For example, in March 2020, CANbridge advised us that it is evaluating alternative development plans for AV-203 which will delay the initiation of clinical trials of AV-203. In addition, if any strategic partner were to breach or terminate its arrangements with us, the development and commercialization of the affected product candidate could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of the product candidate on our own. Our current partners and licensees can terminate their agreements with us under various conditions, including without cause, at which point they would no longer continue to develop our products. For example, in September 2020 Biodesix exercised its Opt-Out right under the Biodesix Agreement. As a result, Biodesix is not required to contribute to the future development costs of ficlatuzumab in exchange for a reduced economic interest in any future ficlatuzumab revenues.

Much of the potential revenue from any of our strategic partnerships will likely consist of contingent payments, such as development milestones and royalties payable on sales of any successfully developed drugs. Any such contingent revenue will depend upon our, and our strategic partners', ability to successfully develop, introduce, market and sell new drugs. In some cases, we are not involved in these processes, and we depend entirely on our strategic partners. Any of our strategic partners may fail to develop or effectively commercialize these drugs because it:

- decides not to devote the necessary resources because of internal constraints, such as limited personnel with the requisite scientific expertise, limited cash resources or specialized equipment limitations, or the belief that other product candidates may have a higher likelihood of obtaining regulatory approval or may potentially generate a greater return on investment;
- does not have sufficient resources necessary to carry the product candidate through clinical development, regulatory approval and commercialization; or
- cannot obtain the necessary regulatory approvals.

If one or more of our strategic partners fails to develop or effectively commercialize product candidates for any of the foregoing reasons or any other reason, we may not be able to replace the strategic partner with another partner to develop and commercialize a product candidate under the terms of the strategic partnership. We may also be unable to obtain, on terms acceptable to us, a license from such strategic partner to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

Risks Related to Our Intellectual Property Rights

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates, or the scope of our patent protection could be insufficiently broad, which could result in competition and a decrease in the potential market share for our product candidates.

We cannot be certain that patents will be issued or granted with respect to applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The scope of patent protection that the USPTO will grant with respect to the antibodies in our antibody product pipeline is uncertain. It is possible that the USPTO will not allow broad antibody claims that cover closely related antibodies as well as the specific antibody. Upon receipt of FDA approval, competitors would be free to market antibodies almost identical to ours, including biosimilar antibodies, thereby decreasing our market share.

If we do not obtain patent term extensions under the Hatch-Waxman Act and similar non-U.S. legislation to extend the term of patents covering each of our product candidates, our business may be materially harmed.

Patents have a limited duration. The term of a U.S. patent, if granted from an application filed on or after June 8, 1995, is generally 20 years from its earliest U.S. non-provisional filing date. Even if patents covering our product candidates are obtained, once the patents expire, we may be open to competition from competitive medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned or in-licensed patent rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the circumstances, the term of our owned and in-licensed patent rights that cover our product candidates may be extended in the United States under the Hatch-Waxman Act, by supplementary perfection certificates, or SPCs, in certain European countries, and by similar legislation in other countries for delays incurred when seeking marketing approval for a drug candidate. For example, the Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within the applicable deadline, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be materially reduced.

The U.S. patents covering the tivozanib molecule and its therapeutic use are scheduled to expire in 2022. In view of the length of time tivozanib has been under regulatory review at the FDA, however, a patent term extension of up to 5 years may be available, which, if granted, could extend the patent term until 2027. However, the length of the extension could be less than we request, or no extension may be granted at all. Currently, SPCs have been granted in Finland, France, Germany, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Spain and Sweden that extend the term of the corresponding patents that cover the tivozanib molecule in each of those jurisdictions up to 2027. The remaining pending applications for SPCs in Belgium, Denmark and Great Britain may not be similarly granted, or may be granted for a shorter period than requested. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the period of time during which the patent rights covering tivozanib or its use can be enforced will be shortened, and our competitors may obtain approval to market a competing product sooner. As a result, our potential revenue from tivozanib could be materially reduced, causing material harm to our business.

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in patent office proceedings, or in court.

If we or one of our strategic partners were to initiate legal proceedings against a third party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet one or more statutory requirements for patentability, including, for example, lack of novelty, obviousness, lack of written description or non-enablement. In addition, patent validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term, including a patent term adjustment granted by the USPTO, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Additionally, third parties are able to challenge the validity of issued patents through administrative proceedings in the patent offices of certain countries, including the USPTO and the European Patent Office. Although we have conducted due diligence on patents we have exclusively in-licensed, and we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one of our products. Such a loss of patent protection could have a material adverse impact on our business.

Claims that our platform technologies, our products or the sale or use of our products infringe the patent rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

We cannot guarantee that our platform technologies, our products, or the use of our products, do not infringe third-party patents. Third parties might allege that we are infringing their patent rights or that we have misappropriated their trade secrets. Such third parties might resort to litigation against us. The basis of such litigation could be existing patents or patents that issue in the future.

It is also possible that we failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products.

With regard to ficlatuzumab, we are aware of two separate families of United States patents and foreign counterparts, with each of the two families being owned by a different third party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. In the event that the owner of one or more of these patents were to bring an infringement action against us, we may have to argue that our product, its manufacture or use does not infringe a valid claim of the patent in question. Furthermore, if we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on commercially acceptable terms, or at all. Even if we or our strategic partners were able to obtain a license, the rights may be non-exclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time-consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business.

Unfavorable outcomes in an intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.

If third parties successfully assert intellectual property rights against us, we might be barred from using aspects of our technology platform, or barred from developing and commercializing related products. Prohibitions against using specified technologies, or prohibitions against commercializing specified products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations of patent infringement or misappropriation of trade secrets, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the patent owner in order to continue our research and development programs or our partnerships or to market our product(s). It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. This could limit our research and development activities, our ability to commercialize specified products, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market.

In addition, any future patent litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or our strategic partners to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all.

An intellectual property litigation could lead to unfavorable publicity that could harm our reputation and cause the market price of our common stock to decline.

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. In such event, the market price of our common stock may decline.

AV-380 and tivozanib are protected by patents exclusively licensed from other companies or institutions. If the licensors terminate the licenses or fail to maintain or enforce the underlying patents, our competitive position would be harmed and our partnerships could be terminated.

Certain of our product candidates and out-licensing arrangements depend on patents and/or patent applications owned by other companies or institutions with which we have entered into intellectual property licenses. In particular, we hold exclusive licenses from St. Vincent's for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which we refer to as GDF15 and which we use in our AV-380 program, and from KKC for tivozanib. We may enter into additional license agreements as part of the development of our business in the future. Our licensors may not successfully prosecute certain patent applications which we have licensed and on which our business depends or may prosecute them in a manner not in the best interests of our business. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third-party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability. In addition, in spite of our best efforts, a licensor could claim that we have materially breached a license agreement and terminate the license, thereby removing our or our licensees' ability to obtain regulatory approval for and to market any product covered by such license. If these in-licenses are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, identical products. In addition, the partners to which we have sublicensed certain rights under these licenses, such as EUSA, would likely have grounds for terminating our partnerships if these licenses are terminated or the underlying patents are not maintained or enforced. This could have a material adverse effect on our results of operations, our competitive business position and our business prospects.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to patents, we rely on trade secrets, technical know-how, and proprietary information concerning our business strategy in order to protect our competitive position. In the course of our research, development and business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to potential strategic partners. In addition, each of our employees is required to sign a confidentiality agreement upon joining our company. We take steps to protect our proprietary information, and we seek to carefully draft our confidentiality agreements to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures.

Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Our research and development strategic partners may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively and result in a material disruption of our product development programs.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our partners or fraudulently induce our employees or employees of our partners to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and computer viruses, cyber-attacks, or other system failures. Any system failure, accident or security breach that causes interruptions in our operations, for us or our partners, could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and we could incur significant increases in costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our partners occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Additionally, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

Intellectual property rights may not address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds or antibodies that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.

- We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- Our pending patent applications might not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with a competitive advantage; for example, our issued patents may not be broad enough to prevent the commercialization of competitive antibodies that are biosimilar to one or more of our antibody products, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our or our strategic partners' existing or potential commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, several events in the last decade have increased uncertainty with regard to our ability to obtain patents in the future and the value of patents once obtained. Among these, in September 2011, patent reform legislation passed by Congress was signed into law in the United States. The patent law introduced changes including a first-to-file system for determining which inventors may be entitled to receive patents, and post-grant challenges, such as inter-partes review and post-grant review proceedings that allow third parties to challenge newly issued patents. The burden of proof required for challenging a patent in these proceedings is lower than in district court litigation, and patents in the biopharmaceutical industry have been successfully challenged using these new post-grant challenges. In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in specified circumstances or weakening the rights of patent owners in specified situations. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could further weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, and by the EMA and comparable regulatory authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. For example, in June 2013, the FDA issued the 2013 CRL informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial. Further, in January 2019, the FDA recommended that we not submit an NDA for tivozanib at that time as the first interim OS results from the TIVO-3 trial did not allay its concerns about a potential detriment in OS from the TIVO-1 trial. In August 2019, we performed a second prespecified interim OS analysis. After receiving the results of the second OS analysis, on the recommendation of the FDA, we withheld our NDA filing until March 2020, in order that it would be filed closer to the May 2020 third and final OS analysis. In May 2020, we performed a final OS analysis, and in June 2020, the FDA accepted our NDA filing for substantive review, setting a PDUFA target date of March 31, 2021. If the FDA does not find that the results of the TIVO-3 trial and the earlier tivozanib clinical trials adequately demonstrate a favorable risk-benefit profile for tivozanib in RCC, we may not be able to obtain marketing approval from the FDA to commercialize tivozanib in the United States.

In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions. In order to market and sell our medicines in the EU and many other jurisdictions, we or our collaborators must obtain marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any particular market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the EU have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or the EU for our product candidates, which could significantly and materially harm our business.

We may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates, and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We or our collaborators may seek orphan drug designations for other product candidates and may be unable to obtain such designations.

Even if we obtain orphan drug designation for a product candidate, we may not be able to obtain orphan drug exclusivity for that candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug or biologic for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Even if we or our collaborators obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We and our collaborators must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our collaborators and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, were we to receive marketing approval for one or more of our product candidates, we would continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we and our collaborators are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements, when and if any of them are approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers’ communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

The efforts of the Trump Administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. For example, on January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that required that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that required the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the Trump Administration indicated that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations. More recently, on October 9, 2019, the President issued another executive order, the "Executive Order on Promoting the Rule of Law Through Improved Agency Guidance Documents." The order is meant to ensure that agency guidance documents do not establish legally binding requirements and it directs each agency to rescind guidance documents that it determines should no longer be in effect. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $11,181 to $22,363 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to annually report to Centers for Medicare and Medicaid Services, or CMS, (i) payments and other transfers of value to physicians and teaching hospitals, and (ii) certain physician ownership or investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require manufacturers to report information related to payments and other transfers of value to other healthcare providers and healthcare entities, or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from funded healthcare programs and the curtailment or restructuring of our operations. Any such penalties could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. One such executive order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. A second executive order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General have filed suit to stop the Trump Administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. On June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. On April 27, 2020, however, the United States Supreme Court reversed the federal circuit decision upholding Congress' denial of such risk corridor funding.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or TCJA, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise.
On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration thereafter represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. In those arguments, the Trump Administration argued in support of upholding the lower court decision. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. On March 3, 2020, that court agreed to hear this case. On June 25, 2020, the Trump Administration and a coalition of 18 states asked the court to strike down the entirety of the ACA. Oral argument in the case is scheduled for November 10, 2020. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, the current presidential administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs.

In addition, CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre-authorization and step therapy for six protected classes of drugs, with certain exceptions, permit plans to implement pre-authorization and step therapy in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business.

More recently, on July 24, 2020, the President issued four executive orders intended to lower the costs of prescription drug products. The first order would require all federally qualified health centers, or FQHCs, to pass on to patients the discounts the health centers receive on insulin and epinephrine through Medicare's 340B Drug Discount Program. The second order would establish an international pricing index that would set the price Medicare Part B pays for the costliest medications covered under the program to the lowest price in other economically advanced countries.

The third order was intended to reduce the costs of drugs by supporting the safe importation of prescription drugs. Specifically, the order calls upon the Department of Health and Human Services, or HHS, to facilitate grants to individuals of waivers of the prohibition of importation of prescription drugs that would allow patients to import FDA approved drug products from abroad, so long as doing so would result in lower costs. In addition, the order would allow wholesalers and pharmacies to re-import both biological drugs and insulin that were originally manufactured in the United States and then exported for international sale. This action preceded the finalization of a rulemaking on September 24, 2020 that allows states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

The fourth order would end drug rebates used by health plan sponsors, pharmacies or pharmacy benefit managers, or PBMs, in operating the Medicare Part D program. Specifically, the order directs HHS to exclude from safe harbor protections under the federal anti-kickback statute retroactive price reductions that are not applied at the point-of-sale. Instead, the order requires HHS to establish new safe harbors that would allow health plan sponsors, pharmacies, and PBMs to pass on those discounts to consumers at point-of-sale in order to lower the patient's out-of-pocket costs and permit the use of certain bona fide PBM service fees. Each of these orders directs the federal government to implement the initiatives outlined in the orders, meaning they will not have immediate effects.

Following issuance of these orders, the President issued a fifth executive order which instructs the federal government to develop a list of "essential" medicines and then buy them and other medical supplies from U.S. manufacturers instead of from companies around the world, including especially China. The order is meant reduce regulatory barriers to domestic pharmaceutical manufacturing and catalyze manufacturing technologies needed to keep drug prices low and the production of drug products in the United States.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Disruptions at the FDA and other government agencies could prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

Disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Employee Matters and Managing Potential Growth

If we fail to attract and keep senior management, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management personnel. We are highly dependent upon our senior management, as well as others on our management team. The loss of services of employees, and in particular, of a member of management could delay or prevent our ability to successfully maintain or enter into new licensing arrangements or collaborations, the successful development of our product candidates, the completion of our planned clinical trials or the commercialization of our product candidates. We do not carry "key person" insurance covering any members of our senior management. Our employment arrangements with all of these individuals are "at will," meaning they or we can terminate their service at any time.

We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. We may face challenges in retaining our existing senior management and key employees and recruiting new employees to join our company as our business needs change. In addition, the COVID-19 pandemic may negatively impact our ability to recruit and build out our organization as planned. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our future business plans.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health-care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. Despite the adoption of an insider trading policy, we may not be able to prevent a director, executive or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Risks Related to Ownership of Our Common Stock

If we fail to meet the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed for quotation on the Nasdaq Capital Market. We are required to meet specified requirements to maintain our listing on the Nasdaq Capital Market, including, among other things, a minimum bid price of $1.00 per share. On March 18, 2019, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Capital Market. On February 19, 2020, we effected a 1-for-10 reverse stock split of our common stock seeking to regain compliance with Nasdaq's continued listing standards. As a result of the reverse stock split, the split-adjusted per share market price of our common stock increased and on March 5, 2020, we received a notice from Nasdaq indicating that we have regained compliance with Listing Rule 5450(a)(1) as of such date.

Although we currently comply with the minimum bid requirement following the reverse stock split, our bid price could fall below $1.00 per share again in the future, in which event we would receive another deficiency notice from Nasdaq advising us that we have 180 days to regain compliance by maintaining a minimum bid price of at least $1.00 for a minimum of ten consecutive business days. Under certain circumstances, Nasdaq could require that the minimum bid price exceed $1.00 for more than ten consecutive days before determining that a company complies. If we fail to satisfy the Nasdaq Capital Market's continued listing requirements, we may transfer to the OTC Bulletin Board. Having our common stock trade on the OTC Bulletin Board could adversely affect the liquidity of our common stock. Any such transfer could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, any of which may contribute to a further decline in our stock price.

The market price of our common stock has been, and is likely to be, highly volatile, and could fall below the price you paid. A significant decline in the value of our stock price could also result in securities class-action litigation against us.

The market price of our common stock has been, and is likely to continue to be, highly volatile and subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

- new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials;
- the effect of the COVID-19 outbreak on the healthcare system and the economy generally and on our clinical trials and other operations specifically;
- the results of regulatory reviews and other regulatory correspondence relating to our product candidates or our clinical trials;
- the results of our efforts to develop, acquire or in-license additional product candidates or products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us of material developments in our business, financial condition and/or operations;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;
- general economic and market conditions, such as the impact of the COVID-19 pandemic on our industry and market conditions, and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

Periods of volatility in the market for a company's stock are often followed by litigation against the company. For example, following our failure to obtain FDA approval for tivozanib in 2013, we and certain of our former officers and directors were involved in several legal proceedings. Following our January 2019 announcement that the FDA did not recommend we file an NDA for tivozanib at that time, several lawsuits were filed against us, our directors, and certain of our current and former officers. See Part II, Item 1 of this Quarterly Report on Form 10-Q under the heading "Legal Proceedings." While the 2019 Class Action was dismissed, any litigation instituted against us in the future could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

We and our collaborators may not achieve development and commercialization goals in the estimated time frames that we publicly announce, which could have an adverse impact on our business and could cause our stock price to decline.

We set goals, and make public statements regarding our expected timing for certain accomplishments, such as statements we have made about the initiation and completion of clinical trials, filing and approval of regulatory applications and other developments and milestones under our research and development programs and those of our partners and collaborators for tivozanib, ficlatuzumab, AV-203, AV-380 and AV-353. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, delays or failures in our preclinical studies or clinical trials, insufficient data or unsatisfactory results from trials, the amount of time, effort and resources committed to our programs and the uncertainties inherent in the regulatory approval process. As a result, there can be no assurance that our preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we will make regulatory submissions or receive regulatory approvals as planned or that we will be able to adhere to our currently anticipated schedule for the achievement of key milestones under any of our programs. If we fail to achieve one or more of the events described above as planned, our business could be materially adversely affected and the price of our common stock could decline.

Our management has broad discretion over our use of available cash and cash equivalents and might not spend our available cash and cash equivalents in ways that increase the value of your investment.

Our management has broad discretion on where and how to use our cash and cash equivalents and you will be relying on the judgment of our management regarding the application of our available cash and cash equivalents to fund our operations. Our management might not apply our cash and cash equivalents in ways that increase the value of your investment. We expect to use a substantial portion of our cash to fund existing and future research and development of our preclinical and clinical product candidates, with the balance, if any, to be used for working capital and other general corporate purposes, which may in the future include investments in, or acquisitions of, complementary businesses, joint ventures, partnerships, services or technologies. Our management might not be able to yield a significant return, if any, on any investment of this cash. You will not have the opportunity to influence our decisions on how to use our cash reserves.

Fluctuations in our quarterly operating results could adversely affect the price of our common stock.

Our quarterly operating results may fluctuate significantly. Some of the factors that may cause our operating results to fluctuate on a period-to-period basis include:

- the status of our clinical development programs;
- the level of expenses incurred in connection with our clinical development programs, including development and manufacturing costs relating to our clinical development candidates;
- the implementation of restructuring and cost-savings strategies;
- the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement;
- costs associated with lawsuits against us or other litigation in which we may become involved, including the current lawsuits described elsewhere in this Quarterly Report on Form 10-Q under “Part II, Item 1 – Legal Proceedings”;
- changes in our 2017 Loan Agreement or 2020 Loan Amendment with Hercules, including the existence of any event of default that may accelerate then remaining principal payments and fees due thereunder;
- non-cash changes in fair value related to re-valuations of our outstanding warrant liability as a result of fluctuations in our stock price; and
- compliance with regulatory requirements.

In addition, in March 2020, we decided to discontinue our CyFi-2 trial of ficlatuzumab due to the urgent shift in priorities among clinical trial sites towards efforts to combat the COVID-19 pandemic, which has impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial supply. While the COVID-19 pandemic has not had a material adverse impact on our operations to date, the future impact of COVID-19 is highly uncertain and cannot be predicted and there is no assurance that the outbreak will not have a material adverse impact on our future operations. The extent of the impact, if any, will depend on future developments, including the extent of the pandemic and governmental actions taken to contain the COVID-19 pandemic.

Period-to-period comparisons of our historical and future financial results may not be meaningful, and investors should not rely on them as an indication of future performance. Our fluctuating results may fail to meet the expectations of securities analysts or investors. Our failure to meet these expectations may cause the price of our common stock to decline.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have been experiencing extreme volatility and disruptions in 2020 due to the COVID-19 pandemic and the government measures taken in response to the pandemic. We expect that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will continue. Our general business strategy may be adversely affected by external economic conditions and a volatile business environment or unpredictable and unstable market conditions. If the equity and credit markets are not favorable at any time we seek to raise capital, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or other partners may not survive economically turbulent times, which could directly affect our ability to attain our operating goals on schedule and on budget.

At September 30, 2020, we had approximately $68.8 million of cash, cash equivalents and marketable securities, consisting of cash on deposit with banks, a U.S. government money market fund and high-grade debt securities, including short-term commercial paper, corporate bonds and other U.S. government agency securities. As of the date of this report, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or marketable securities. However, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents and marketable securities or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents and marketable securities owned by us.

Future sales of shares of our common stock, including shares issued upon the exercise of currently outstanding options and warrants, could negatively affect our stock price.

A substantial portion of our outstanding common stock can be traded without restriction at any time. Some of these shares are currently restricted as a result of securities laws, but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock. In addition, we have a significant number of shares that are subject to outstanding options and warrants. The exercise of these options or warrants and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock may depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. A lack of research coverage may negatively impact the market price of our common stock. To the extent we do have analyst coverage, if one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

A decline in our stock price may affect future fundraising efforts.

We currently have no product revenues, and depend entirely on funds raised through other sources. One source of such funding is future debt and/or equity offerings. Our ability to raise funds in this manner depends upon, among other things, our stock price, which may be affected by capital market forces, evaluation of our stock by securities analysts, product development success (or failure), and internal management operations and controls.

Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Provisions of our certificate of incorporation, our by-laws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the ability of our board of directors to make, alter or repeal our by-laws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that a stockholder could receive a premium for shares of our common stock held by a stockholder in an acquisition.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

- responding to proxy contests and other actions by activist stockholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;
- perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls, and requires our independent registered public accounting firm to attest to the effectiveness of our internal controls. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm's, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we are unable to successfully remediate any material weaknesses in our internal control, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our stock price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC, or other regulatory authorities.

We do not expect to pay any cash dividends for the foreseeable future.

Our stockholders should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. In addition, the terms of the 2017 Loan Agreement and 2020 Loan Amendment preclude, and any future debt agreements may preclude us from paying dividends. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the TCJA, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2019, we had federal net operating loss carryforwards of $527.1 million, of which $502.6 million will, if not used, expire at various dates through 2037, and federal research and development tax credit carryforwards of $11.3 million, which will, if not used, expire at various dates through 2039. To the extent that they expire unused, these net operating loss and tax credit carryforwards will not be available to offset our future income tax liabilities.

In general, under Section 382 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss and credit carryforwards to reduce its tax liability for post-change periods may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards is subject to an annual limitation under Section 382. We also may experience ownership changes in the future as a result of shifts in our stock ownership, some of which may be outside of our control. In addition, we have not conducted a detailed study to document whether our historical activities qualify to support the research and development credits currently claimed as a carryforward. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, our use of those attributes to offset future income tax liabilities would be limited.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes.

Item 6. Exhibits.

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated by Reference: Form	Incorporated by Reference: File Number	Date of Filing	Exhibit Number	Filed Herewith
10.1	First Amendment to Amended and Restated Loan and Security Agreement, dated as of August 7, 2020, by and among the registrant, Hercules Capital, Inc. and the other lenders named therein	10Q	001-34655	08/10/2020	10.1	
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.					X
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 Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).					

* Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

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.

AVEO PHARMACEUTICALS, INC.

Date: November 9, 2020

By: /s/ Erick Lucera

Erick Lucera
Chief Financial Officer and Principal Financial and Accounting Officer

Exhibit 31.1

CERTIFICATION

I, Michael Bailey, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, 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 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 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.

Date: November 9, 2020

/s/ Michael Bailey
Michael Bailey
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Erick Lucera, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, 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 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 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.

Date: November 9, 2020

/s/ Erick Lucera
Erick Lucera
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended September 30, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Bailey, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 9, 2020

/s/ Michael Bailey
Michael Bailey
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended September 30, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Erick Lucera, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 9, 2020

/s/ Erick Lucera
Erick Lucera
Chief Financial Officer
(Principal Financial Officer)