AVEO PHARMACEUTICALS INC
Form 10-Q
November 09, 2018

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, 2018

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.)

One Broadway, 14th Floor, Cambridge, Massachusetts 02142

(Address of Principal Executive Offices) (Zip Code)

(617) 588-1960

(Registrant's Telephone Number, Including Area Code)

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. (Check one):

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 8, 2018: 125,346,598

AVEO PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE QUARTER ENDED SEPTEMBER 30, 2018

TABLE OF CONTENTS

		Page No.
PART I. FINANCIAL INFORMATION		
Item 1.	Financial Statements	
	Condensed Consolidated Balance Sheets as of September 30, 2018 and December 31, 2017	3
	Condensed Consolidated Statements of Operations for the Three and Nine Months Ended September 30, 2018 and 2017	4
	Condensed Consolidated Statements of Comprehensive Loss for the Three and Nine Months Ended September 30, 2018 and 2017	5
	Condensed Consolidated Statements of Cash Flows for the Nine Months Ended September 30, 2018 and 2017	6
	Notes to Condensed Consolidated Financial Statements	7
Item 2.	Management's Discussion and Analysis of Financial Condition and Results of Operations	36
Item 3.	Quantitative and Qualitative Disclosures About Market Risk	60
Item 4.	Controls and Procedures	60
PART II. OTHER INFORMATION		
Item 1.	Legal Proceedings	61
Item 1A.	Risk Factors	62
Item 6.	Exhibits	95
	Signatures	97

2

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets

(In thousands, except par value amounts)

(Unaudited)

	September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 20,408	$ 14,949
Marketable securities	—	18,576
Accounts receivable	344	402
Insurance recovery (Note 9)	—	15,000
Clinical trial retainers	284	1,027
Other prepaid expenses and other current assets	402	229
Total current assets	21,438	50,183
Other assets	4	15
Total assets	$ 21,442	$ 50,198
Liabilities and stockholders' deficit		
Current liabilities:		
Accounts payable	$ 2,983	$ 2,436
Accrued clinical trial costs and contract research	7,253	8,321
Other accrued liabilities	3,190	2,458
Loans payable, net of discount	4,256	—
Deferred revenue	1,342	395
Deferred research and development reimbursements	463	901
Estimated settlement liability (Note 9)	—	17,073
Other liabilities (Note 6)	—	540
Total current liabilities	19,487	32,124
Loans payable, net of current portion and discount	14,621	18,477
Deferred revenue	3,414	1,302
Deferred research and development reimbursements	65	222
PIPE Warrant liability (Note 7)	43,157	37,746
Other liabilities (Note 6)	1,090	1,090
Total liabilities	81,834	90,961
Stockholders' deficit:		
Preferred stock, $.001 par value: 5,000 shares authorized at September 30, 2018 and December 31, 2017; no shares issued and outstanding at each of September 30, 2018 and December 31, 2017	—	—
Common stock, $.001 par value: 250,000 shares authorized at September 30,	121	118

2018 and December 31, 2017; 121,539 and 118,325 shares issued and outstanding as of September 30, 2018 and December 31, 2017, respectively		
Additional paid-in capital	556,314	546,092
Accumulated other comprehensive loss	—	(4)
Accumulated deficit	(616,827)	(586,969)
Total stockholders' deficit	(60,392)	(40,763)
Total liabilities and stockholders' deficit	$ 21,442	$ 50,198

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations

(In thousands, except per share amounts)

(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Revenues:				
Collaboration and licensing revenue	$2,335	$4,614	$3,651	$7,497
Partnership royalties	132	—	275	—
	2,467	4,614	3,926	7,497
Operating expenses:				
Research and development	5,160	4,666	15,451	19,503
General and administrative	2,719	2,101	8,156	6,734
Settlement costs (Note 9)	—	—	(667)	—
	7,879	6,767	22,940	26,237
Loss from operations	(5,412)	(2,153)	(19,014)	(18,740)
Other expense, net:				
Interest expense, net	(579)	(655)	(1,621)	(1,736)
Change in fair value of PIPE Warrant liability	(16,172)	(23,538)	(6,512)	(47,947)
Other expense, net	(16,751)	(24,193)	(8,133)	(49,683)
Loss before provision for income taxes	(22,163)	(26,346)	(27,147)	(68,423)
Provision for income taxes	—	(51)	—	(101)
Net loss	$(22,163)	$(26,397)	$(27,147)	$(68,524)
Net loss per share - basic and diluted	$(0.18)	$(0.22)	$(0.23)	$(0.67)
Weighted average number of common shares outstanding – basic and diluted	120,138	118,006	119,311	101,754

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss

(In thousands)

(Unaudited)

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2018	2017	2018	2017
Net loss	$(22,163)	$(26,397)	$(27,147)	$(68,524)
Other comprehensive loss:				
Unrealized gain (loss) on available-for-sale securities	(1)	4	4	(4)
Comprehensive loss	$(22,164)	$(26,393)	$(27,143)	$(68,528)

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows

(In thousands)

(Unaudited)

	Nine Months Ended September 30,	
	2018	2017
Operating activities		
Net loss	$(27,147)	$(68,524)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	1,888	774
Non-cash interest expense	399	391
Non-cash change in fair value of PIPE Warrant liability	6,512	47,947
Non-cash charge for settlement costs (Note 9)	(667)	—
Amortization of premium and discount on investments	3	36
Changes in operating assets and liabilities:		
Accounts receivable	58	(1,348)
Insurance recovery (Note 9)	15,000	—
Prepaid expenses and other current assets	570	196
Other noncurrent assets	11	787
Accounts payable	547	(245)
Accrued contract research	(1,068)	3,498
Other accrued liabilities	732	90
Settlement liability (Note 9)	(15,000)	—
Deferred revenue	348	(411)
Deferred research and development reimbursements	(595)	1,394
Net cash used in operating activities	(18,409)	(15,415)
Investing activities		
Purchases of marketable securities	(6,733)	(27,793)
Proceeds from maturities and sales of marketable securities	25,312	14,950
Net cash provided by (used in) investing activities	18,579	(12,843)
Financing activities		
Proceeds from issuance of common stock, net of issuance costs	1,100	21,294
Proceeds from issuance of common stock to related parties	4,500	3,210
Proceeds from issuance of stock for stock-based compensation arrangements	229	12
Proceeds from issuance of loans payable	—	5,000
Payment of end-of-term loan costs (Note 6)	(540)	—
Net cash provided by financing activities	5,289	29,516
Net increase in cash and cash equivalents	5,459	1,258
Cash and cash equivalents at beginning of period	14,949	15,096
Cash and cash equivalents at end of period	$20,408	$16,354
Supplemental cash flow information		

Cash paid for interest	$1,486	$1,468
Non-Cash Operating Activity		
Increase to deferred revenue due to adoption of ASC Topic 606 - transition adjustment on January 1, 2018	$2,711	$—

See accompanying notes.

AVEO Pharmaceuticals, Inc.

Notes to Condensed Consolidated Financial Statements

September 30, 2018

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is a biopharmaceutical company dedicated to advancing a broad portfolio of targeted medicines for oncology and other areas of unmet medical need. The Company's strategy is to retain North American rights to its oncology portfolio while securing partners in development and commercialization outside of North America. The Company is working to develop and commercialize its lead candidate tivozanib in North America as a treatment for advanced or metastatic renal cell carcinoma ("RCC"). On November 5, 2018, the Company announced positive topline results from the primary analysis of the Company's phase 3 trial of tivozanib in the third- and fourth-line treatment of patients with RCC (the "TIVO-3 trial"), a randomized, controlled, multi-center, open-label study to compare tivozanib to sorafenib (Nexavar®), an approved therapy, in 351 subjects with RCC. The TIVO-3 trial met its primary endpoint for progression-free survival ("PFS"). The analysis of the secondary endpoint of overall survival ("OS") was not mature at the time of the final PFS analysis. Based on the results of the TIVO-3 trial, together with the previously completed phase 3 trial of tivozanib in the first line treatment of RCC (the "TIVO-1 trial"), the Company plans to submit a New Drug Application ("NDA") to the U.S. Food and Drug Administration ("FDA") within approximately six months from its announcement of topline data results of the TIVO-3 trial. The Company has outlicensed tivozanib (FOTIVDA®) for oncological indications in Europe and other territories outside of North America, and it is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with RCC and for adult patients who are vascular endothelial growth factor receptor ("VEGFR") and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. The Company has entered into partnerships to fund the development and commercialization of AV-203 and ficlatuzumab, both clinical stage assets in oncology. The Company is currently seeking a partner to develop the AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension ("PAH") and oncology. In addition, a new formulation of tivozanib is being explored in ocular conditions. The Company has recently regained the rights to its AV-380 program for the potential treatment of cachexia and is considering a variety of options to advance the program's development.

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

Liquidity and Going Concern

The Company has financed its operations to date 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. As of September 30, 2018, the Company had cash, cash equivalents and marketable securities totaling approximately $20.4 million, working capital of $2.0 million and an accumulated deficit of $616.8 million.

The Company is subject to a number of risks, including the need for substantial additional capital for clinical research and product development. As of September 30, 2018, the Company had approximately $20.4 million in cash, cash equivalents and marketable securities. In the fourth quarter of 2018 to-date, the Company sold approximately 3.8 million shares of its common stock pursuant to its sales agreement with Leerink Partners LLC (the "Leerink Sales Agreement") and received approximately $8.4 million in net proceeds. Based on these available cash resources, the Company does not have sufficient cash on hand to support current operations for at least the next 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 with EUSA Pharma (UK) Limited (the "EUSA Agreement"). In August 2017, EUSA Pharma (UK) Limited ("EUSA") obtained marketing approval from the European Medicines Agency (the "EMA") for tivozanib (FOTIVDA) for the treatment of RCC.

- 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 sales 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 discussed in Note 7.
- Partner AV-353 to secure potential additional non-dilutive funds and advance development of the AV-353 platform for the potential treatment of PAH.

Pursuant to the EUSA Agreement, the Company is entitled to receive up to an additional $8.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy and Spain, 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, as mutually agreed by the parties. These milestone payments are subject to the 30% sublicense fee payable to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.) ("KHK") pursuant to the Company's license agreement with KHK (the "KHK Agreement"). 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 TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that study. This research and development reimbursement payment would not be subject to the 30% sublicense fee payable to KHK, subject to certain limitations. Refer to Note 4 "Collaborations and License Agreements - KHK" for further details.

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 at least the next twelve months from the date of filing this Quarterly Report on Form 10-Q.

Pursuant to the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern ("ASC 205-40") management must evaluate whether there are conditions or 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 financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, 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 other resources 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.

The Company believes that its approximate $20.4 million in cash, cash equivalents and marketable securities at September 30, 2018, along with approximately $8.4 million received in net proceeds from the sale of approximately 3.8 million shares of its common stock pursuant to the Leerink Sales Agreement in the fourth quarter of 2018 to-date, would allow it to fund its planned operations into the second quarter of 2019. This estimate assumes no receipt of additional milestone payments from its partners, no funding from new partnership agreements, no additional equity financings, no debt financings, no additional sales of equity under the Leerink Sales Agreement and no additional sales of equity through the exercise of the outstanding PIPE Warrants or the Settlement Warrants (Refer to Note 7,

Common Stock – Settlement Warrants and Private Placement / PIPE Warrants regarding specific details.). Accordingly, the timing and nature of activities contemplated for the remainder of 2018, 2019 and thereafter will be conducted subject to the availability of sufficient financial resources.

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 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 10 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 months and nine months ended September 30, 2018 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2018 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at September 30, 2018, and for the three months and nine months ended September 30, 2018 and 2017, is unaudited, and the condensed consolidated balance sheet amounts and related footnotes as of December 31, 2017 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, 2017, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 13, 2018.

(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

Effective January 1, 2018, the Company adopted ASC 606 using the modified retrospective transition method. Under this method, the Company has recognized the cumulative effect of the adoption as an adjustment to the opening balance of accumulated deficit in the current period condensed consolidated balance sheet. Financial results for reporting periods beginning after January 1, 2018, are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with the Company's historical accounting under ASC 605, Revenue Recognition. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements and leases.

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, 2018 and 2017, 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,	
	2018	2017	2018	2017
EUSA	$467	$4,099	$1,926	$4,297
Novartis	—	15	—	1,835
CANbridge	2,000	500	2,000	1,000
Ophthotech	—	—	—	115
Other	—	—	—	250
Total	$2,467	$4,614	$3,926	$7,497

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 internal costs for salaries, bonuses,

benefits, stock-based compensation, facilities, and research-related overhead, and external costs for clinical trials, drug manufacturing and distribution, license fees, consultants and other contracted services.

Warrants Issued in Connection with Private Placement

In May 2016, the Company issued warrants to purchase an aggregate of 17,642,482 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, 2018, PIPE Warrants exercisable for 777,201 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 16,865,281 shares of common stock were outstanding. In July 2017, Hercules Capital Inc. exercised its PIPE Warrants with respect to all 259,067 shares of common stock underlying such PIPE Warrants, and the Company issued Hercules Capital Inc. 259,067 shares of its common stock and received approximately $0.3 million in cash proceeds. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and the Company issued 518,134 shares of its common stock and received approximately $0.5 million in cash proceeds. Refer to Note 7, “Common Stock—Private Placement / PIPE Warrants” 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 non-cash losses of approximately $16.2 million and $6.5 million in the three months and nine months ended September 30, 2018, respectively, and non-cash losses of approximately $23.5 million and $47.9 million in the three months and nine months ended September 30, 2017, respectively, in its Statement of Operations attributable to the increases in the fair value of the PIPE Warrant liability that resulted from higher stock prices as of September 30, 2018 and September 30, 2017 relative to prior periods. In the nine months ended September 30, 2018, the Company recorded a reduction in the PIPE Warrant liability, with a corresponding increase to additional paid-in capital, of approximately $1.1 million attributable to PIPE Warrant exercises in the first quarter of 2018.

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 three months and nine months ended September 30, 2018 (in thousands):

Fair value at January 1, 2018	$37,746
Increase in fair value	1,465
Reduction in warrant liability for PIPE Warrant exercises	(1,101)
Fair value at March 31, 2018	$38,110
Decrease in fair value	(11,125)
Fair value at June 30, 2018	$26,985
Increase in fair value	16,172
Fair value at September 30, 2018	$43,157

The key assumptions used to value the PIPE Warrants were as follows:

	Issuance	December 31, 2017	March 31, 2018	June 30, 2018	September 30, 2018
Expected price volatility	76.25%	84.86%	85.61%	78.27%	78.56%
Expected term (in years)	5.00	3.50	3.25	3.00	2.75
Risk-free interest rates	1.22%	2.09%	2.39%	2.63%	2.88%
Stock price	$ 0.89	$ 2.79	$ 2.90	$ 2.26	$ 3.31

Dividend yield	—	—	—	—	—

Class Action Settlement and Settlement Warrants

In December 2017, the Company entered into a binding memorandum of understanding (the "MOU") with class representatives Bob Levine and William Windham (the "Plaintiffs"), regarding the settlement of a securities class action lawsuit (the "Class Action") that had been filed in 2013 and was pending in the United States District Court for the District of Massachusetts (the "District Court") against the Company and certain of the Company's former officers (Tuan Ha-Ngoc, David Johnston, and William Slichenmyer, together, the "Individual Defendants"), In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC. As previously disclosed, the Class Action was purportedly brought on behalf of stockholders who purchased the Company's common stock between May 16, 2012 and May 1, 2013 (the "Class").

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 fair value on December 31, 2017 of 2.0 million warrants to purchase shares of its common stock that the Company agreed to issue the Class (the "Settlement Warrants"), with a corresponding non-cash charge to the Statement of Operations as a component of operating expense. The Settlement Warrants are

exercisable for a one-year period from their date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share.

The settlement was subject to the execution of a definitive settlement agreement, notice to the Class, and final approval of the District Court and became effective on the date (the "Effective Date") on which all of the following conditions occurred: (a) a final judgment containing the requisite release of claims had been entered by the District Court; (b) no appeal was pending with respect to the final judgment; (c) the final judgment had not been reversed, modified, vacated or amended; (d) the time to file any appeal from the final judgment had expired without the filing of an appeal or an order dismissing the appeal or affirming the final judgment had been entered, and any time to file a further appeal (including a writ of certiorari or for reconsideration of the appeal) had expired; and (e) the MOU and any settlement agreement with respect to the claims released in the final judgment had not expired or been terminated.

In January 2018, the Company entered into a definitive stipulation of settlement agreement (the "Stipulation"). In February 2018, the District Court preliminarily approved the Stipulation, following which the insurance carriers funded the settlement escrow account related to the $15.0 million cash portion of the settlement. On May 30, 2018, the District Court approved the Stipulation in its order of final approval and final judgment (the "Final Judgment"). Upon the conclusion of a 30-day appeal period, the Effective Date was deemed to be June 29, 2018. 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 $15.0 million contingent liability associated with the cash portion of the settlement and the corresponding insurance recovery were eliminated on the Effective Date. The Company had agreed to use its best efforts to issue and deliver the Settlement Warrants within ten business days following the Effective Date. On July 16, 2018, the Company issued and delivered the Settlement Warrants in accordance with the Stipulation and filed a corresponding shelf registration statement, File No. (333-226190) to register the shares of common stock underlying the Settlement Warrants which was declared effective by the SEC on July 25, 2018.

Refer to Note 9, "Legal Proceedings" for further discussion of the Class Action settlement.

The estimated fair value of the Settlement Warrants was determined using the Black-Scholes pricing model. The estimated fair value of the Settlement Warrants was subject to revaluation at each balance sheet date and any changes in fair value were recorded as a non-cash gain or (loss) in the Statement of Operations as a component of operating expenses until the Settlement Warrants were issued. In addition, the fair value of the Settlement Warrants on June 30, 2018 was determined based on the estimated fair value of the Settlement Warrants at the time of issuance. The Company recorded non-cash gains of approximately $0.7 million during the nine months ended September 30, 2018 in its Statement of Operations attributable to the decrease in the fair value of the Settlement Warrants prior to their issuance that principally resulted from a lower volatility rate relative to prior periods. In July 2018, upon the issuance of the Settlement Warrants, the Company reclassified the approximate $1.4 million value of the Settlement Warrants from a liability to stockholders equity as a component of additional paid-in-capital based upon the terms of the warrant agreement and, accordingly, the approximate $1.4 million contingent liability on the Company's balance sheet as of June 30, 2018 associated with the warrant portion of the settlement was eliminated.

The key assumptions used to estimate the fair value the Settlement Warrants were as follows:

	December 31, 2017	March 31, 2018	June 30, 2018
Expected price volatility	101.52%	96.01%	62.74%

Expected term (in years)	1.00	1.00	1.00
Risk-free interest rates	1.76%	2.09%	2.37%
Stock price	$ 2.79	$ 2.90	$ 2.90
Dividend yield	—	—	—

Cash and Cash Equivalents

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

Marketable securities consist primarily of investments which have expected average maturity dates in excess of three months, but not longer than 24 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 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 to maturity, 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, 2018 and December 31, 2017 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
September 30, 2018				
Cash and cash equivalents:				
Cash and money market funds	$ 15,360	$ —	$ —	$15,360
Corporate debt securities	3,051	—	—	3,051
U.S. government agency securities	1,997	—	—	1,997
Total cash, cash equivalents and marketable securities	$ 20,408	$ —	$ —	$20,408
December 31, 2017:				
Cash and cash equivalents:				
Cash and money market funds	$ 14,949	$ —	$ —	$14,949
Total cash and cash equivalents	14,949	—	—	14,949
Marketable securities:				
Corporate debt securities due within 1 year	$ 17,074	$ 1	$ (5)	$17,070
U.S. government agency securities due within 1 year	1,506	—	—	1,506
Total marketable securities	$ 18,580	$ 1	$ (5)	$18,576
Total cash, cash equivalents and marketable securities	$ 33,529	$ 1	$ (5)	$33,525

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, 2018, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a U.S. government money market fund and its financial assets valued based on Level 2 inputs consisted of high-grade corporate debt securities, including commercial paper, and U.S. government agency securities. During the three months and nine months ended September 30, 2018, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of September 30, 2018, 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, 2018 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 assets and liabilities measured at fair value on a recurring basis at September 30, 2018 and December 31, 2017 (in thousands):

	Fair Value Measurements as of September 30, 2018			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$15,360	$—	$—	$15,360

Corporate debt securities	—	3,051	—	3,051
U.S. government agency securities	—	1,997	—	1,997
Total cash, cash equivalents and marketable securities	$15,360	$5,048	$—	$20,408
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	$—	$—	$43,157	$43,157

	Fair Value Measurements as of December 31, 2017			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$14,949	$—	$—	$14,949
Total cash and cash equivalents	$14,949	$—	$—	$14,949
Marketable securities:				
Corporate debt securities due within 1 year	$—	$17,070	$—	$17,070
U.S. government agency securities due within 1 year	—	1,506	—	1,506
Total marketable securities	$—	$18,576	$—	$18,576
Total cash, cash equivalents and marketable securities	$14,949	$18,576	$—	$33,525
Financial liabilities carried at fair value:				
PIPE Warrant liability	$—	$—	$37,746	$37,746
Settlement Warrant liability	—	—	2,073	2,073
Total warrant liabilities	$—	$—	$39,819	$39,819

Basic and Diluted Net Income (Loss) per Common Share

Basic net income (loss) per share attributable to AVEO common stockholders is based on the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per share attributable to AVEO 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. Common equivalent shares include the incremental common shares issuable upon the exercise of the PIPE Warrants and the Settlement Warrants, as determined using the treasury stock method. However, for the three months and nine months ended September 30, 2018 and 2017, diluted net loss per share is the same as basic net loss per share as the inclusion of common stock issuable upon the exercise of the PIPE Warrants, Settlement Warrants and other common equivalent stock options, would be anti-dilutive.

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, 2018 and 2017, respectively (in thousands):

	Outstanding at September 30,	
	2018	2017
Options outstanding	9,878	6,970
PIPE Warrants outstanding	16,865	17,383
Settlement Warrants outstanding	2,000	—
Total	28,743	24,353

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 all awards is recognized in the Company's statements of operations over the requisite service period for each award.

Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. Other awards, such as performance-based awards that vest upon the achievement of specified goals, are expensed using the accelerated attribution method if achievement of the specified goals is considered probable. The Company has also granted awards that vest upon the achievement of market conditions. Per ASC 718, Share-Based Payments, market conditions must be considered in determining the estimated grant-date fair value of share-based payments and the market conditions must be considered in determining the requisite service period over which compensation cost is recognized. The Company estimates the fair value of the awards with market conditions using a Monte Carlo simulation, which utilizes several assumptions including the risk-free interest rate, the volatility of the Company's stock and the exercise behavior of award recipients. The grant-date fair value of the awards is then recognized over the requisite service period, which represents the derived service period for the awards as determined by the Monte Carlo simulation.

The Company uses the Black-Scholes option pricing model to value its stock option awards without market conditions, which require 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 are measured at fair value on the date the awards are granted. Awards to nonemployee consultants are recorded at their fair values and are re-measured as of each balance sheet date until the recipient's services are complete. During the three months and nine months ended September 30, 2018 and 2017, the Company recorded the following stock-based compensation expense (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Research and development	$199	$69	$580	$192
General and administrative	485	222	1,308	582
Total	$684	$291	$1,888	$774

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, 2018, the Company is forecasting a net loss for the year ended December 31, 2018 and an effective tax rate of 0%. The Company maintains a full valuation allowance on all deferred tax assets.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which allows the recording of provisional amounts during a measurement period not to extend beyond one year of the enactment date. In accordance with SAB 118, the Company determined a provisional amount for the impact on its prior year deferred tax assets and valuation allowance in its prior year financial statements. The Company's accounting treatment is expected to be completed in the fourth quarter of 2018, within the one-year period from the enactment of the Tax Cuts and Jobs Act.

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, 2018, the Company has 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, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, contract research accruals, measurement of the PIPE Warrant liability, estimated settlement liabilities and measurement of stock-based compensation. 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 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 May 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-09, which amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in ASC 605 and creates ASC 606. In 2015 and 2016, the FASB issued additional ASUs related to ASC 606 that delayed the effective date of the guidance for annual and interim periods beginning after December 15, 2017 and clarified various aspects of the new revenue guidance. ASC Topic 606 also impacts certain other areas, such as the accounting for costs to obtain or fulfill a contract, and requires disclosure of the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers.

On January 1, 2018, the Company adopted ASC 606 using the modified retrospective method and applied the new guidance to the most current period presented with the cumulative effect of changes reflected in the opening balance of accumulated deficit. The Company conducted an analysis with respect to its active revenue arrangements, which at the time included those with EUSA, CANbridge Life Sciences Ltd. ("CANbridge") and Novartis International Pharmaceutical Ltd. ("Novartis").

The adoption of ASC 606 resulted in an approximate $2.7 million increase in each of deferred revenue and the accumulated deficit at the transition date. The transition adjustment related solely to the Company's revenue arrangement with EUSA. The transition adjustment resulted from a change to the Company's accounting policy with respect to the recognition of milestone payments as a result of adopting ASC 606. Prior to the adoption of ASC 606, the Company generally recognized milestone payments in their entirety as revenue in the period the payment was earned. However, under ASC 606, milestone payments are considered to be a form of variable consideration that, upon inclusion in the transaction price, is recognized when (or as) the remaining performance obligation(s) are satisfied. Because the Company's performance obligation under the EUSA Agreement was only partially satisfied at January 1, 2018, a milestone payment received under that arrangement prior to the January 1, 2018 transition date has not been fully recognized as revenue as under ASC 606 as of the transition date.

As a result of adopting ASC 606, the Company established a deferred revenue deferred tax asset, in the amount of $0.7 million, and a corresponding offsetting valuation allowance, such that there was not tax impact on the Company's condensed consolidated financial statements as a result of adopting ASC 606.

There was no impact from adopting ASC 606 to the Company's revenue arrangements with CANbridge and Novartis as (i) the Company did not have any unsatisfied performance obligations under the Company's collaboration and license agreement with CANbridge (the "CANbridge Agreement") and the Company's license agreement with Novartis (the "Novartis Agreement") upon the adoption of ASC 606 and (ii) the transaction price under ASC 606 as of the transition date was the same as the arrangement consideration under ASC Topic 605.

Financial results for reporting periods beginning after January 1, 2018, are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with the Company's historical accounting under ASC 605.

The following table summarizes the cumulative effect of the adoption of ASC 606 to the Company's contracts with customers that were not completed as of the January 1, 2018 transition date (in thousands):

	Impact of ASC 606 Adoption on Condensed Consolidated Balance Sheet as of January 1, 2018		
	As reported under ASC Topic 606	Adjustments	Balances without adoption of ASC Topic 606
Deferred revenue, current portion	$1,027	$ 632	$395
Deferred revenue, net of current portion	$3,381	$ 2,079	$1,302
Accumulated deficit	$(589,680)	$ (2,711)	$(586,969)

The following tables summarize the impact of the adoption of ASC 606 to the Company's condensed consolidated financial statements at September 30, 2018 and for the three months and nine months ended September 30, 2018 as follows (in thousands, except per share figures):

	Impact of ASC 606 Adoption on Condensed Consolidated Balance Sheet as of September 30, 2018		
	As reported under ASC Topic 606	Adjustments	Balances without adoption of ASC Topic 606
Deferred revenue, current portion	$1,342	$ 947	$395
Deferred revenue, net of current portion	$3,414	$ 2,408	$1,006
Accumulated deficit	$(616,827)	$ (3,355)	$(613,472)

	Impact of ASC 606 Adoption on Condensed Consolidated Statement of Operations and Comprehensive Loss					
	Three Months Ended September 30, 2018			Nine Months Ended September 30, 2018		
	As reported under ASC Topic 606	Adjustments	Balances without adoption of ASC Topic 606	As reported under ASC Topic 606	Adjustments	Balances without adoption of ASC Topic 606
Collaboration and licensing revenue	$2,335	$ 237	$2,098	$3,651	$ (645)	$4,296
Total revenues	$2,467	$ 237	$2,230	$3,926	$ (645)	$4,571
Loss before provision for income taxes	$(22,163)	$ 237	$(22,400)	$(27,147)	$ (645)	$(26,502)
Net loss	$(22,163)	$ 237	$(22,400)	$(27,147)	$ (645)	$(26,502)
Net loss per share - basic and diluted	$(0.18)	$ —	$(0.18)	$(0.23)	$ (0.01)	$(0.22)

	Impact of ASC 606 Adoption on Condensed Consolidated Statement of Cash Flows

	as of September 30, 2018		
	As reported under ASC Topic 606	Adjustments	Balances without adoption of ASC Topic 606
Net loss	$(27,147)	$ (645)	$(26,502)
Changes in deferred revenue	$348	$ 645	$(297)

Refer to Note 3 “Significant Accounting Policies – Revenue Recognition” and Note 4 “Collaborations and License Agreements” for further details.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments. The new standard clarifies certain aspects of the statement of cash flows, including the classification of debt prepayment or debt extinguishment costs, settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, proceeds from the settlement of corporate-owned life insurance policies, distributions received from equity method investees and beneficial interests in securitization transactions. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The Company adopted the new standard upon the required effective date of January 1, 2018. The adoption of this standard did not have a material impact on the Company’s consolidated statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. The new standard does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. The new standard is effective for fiscal years, and interim periods within, beginning after December 15, 2017. The Company adopted the new standard effective January 1, 2018. The adoption of this standard did not have a material impact on the Company’s consolidated statements of cash flows.

Pending Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) ("ASU 2016-02"), which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. In July 2018, the FASB issued ASU No. 2018-10, Codification Improvement to Topic 842, Leases ("ASU 2018-10") and ASU No. 2018-11, Leases (Topic 842), Targeted Improvements ("2018-11"). ASU 2018-10 made technical corrections to the new leases standard, clarifying certain inconsistencies in the guidance. ASU 2018-11 provides entities with a new transition method that allows them to use the effective date of the new leases standard as the date of initial application on transition. ASU 2016-02, as modified by ASU 2018-10 and ASU No. 2018-11 will be effective for annual reporting periods beginning after December 15, 2018 with early adoption permitted. The Company is currently evaluating the potential changes from this ASU.

In June 2018, the FASB issued ASU 2018-07, Improvements to Nonemployee Share-Based Payment Accounting, which simplifies the accounting for share-based payments to nonemployees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The new standard is effective for annual reporting periods beginning after December 15, 2018 with early adoption permitted. The Company is currently evaluating the potential changes from this ASU.

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 new standard is effective for the Company on January 1, 2020. Early adoption is permitted. The Company currently is evaluating the impact the adoption of ASU 2018-13 may have on its disclosures.

(4) Collaborations and License Agreements

Out-License Agreements

CANbridge

On March 16, 2016, the Company entered into the CANbridge Agreement. 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 initial new drug ("IND") application with the China National Drug Administration ("CNDA") 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 CNDA and, accordingly, the Company earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018.

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, 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 CNDA 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. Based on this evaluation, the Company identified the following promised goods and services at the inception of the CANbridge Agreement: the Company's grant of an exclusive license to develop and commercialize AV-203 in the CANbridge Licensed Territory, including all technical knowledge and data useful in the development and manufacture of AV-203. The Company determined that the license and know-how represented functional intellectual property. The Company concluded its promise to participate on a joint steering committee was immaterial in the context of the contract based on consideration of qualitative and quantitative factors. In making this evaluation the Company considered the specific personnel and time commitment that would be required to provide the joint steering committee services, concluding that the time commitment would be insignificant. Accordingly, the Company determined the CANbridge Agreement contained a single performance obligation related to the exclusive license to develop and commercialized 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. None of the development and regulatory milestones have been included in the transaction price, as these milestone amounts are 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.

Previously, under ASC 605, the Company recognized the $1.0 million in upfront consideration as collaboration and licensing revenue in the first quarter of 2016 upon delivery of the exclusive license, and recognized the two $0.5 million payments by CANbridge for the reimbursement of manufacturing development activities conducted by the Company prior to the Effective Date as collaboration and licensing revenue in each of March 2017 and September 2017, respectively, as the amounts were fixed, determinable and non-refundable, and the Company did not have any further performance obligations. Accordingly, as the timing and amount of revenue recognition for the payments received from CANbridge are the same under ASC 605 and ASC 606, there was no transition adjustment required as of January 1, 2018.

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 CNDA 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 three months ended September 30, 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 ongoing 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 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"), and an additional $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the European Union, as mutually agreed by the parties. In February 2018, EUSA obtained reimbursement approval from the National Institute for Health and Care Excellence ("NICE") in the United Kingdom for the first-line treatment of RCC. Accordingly, the Company earned a $2.0 million milestone payment that was received in March 2018. 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.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KHK, subject to certain limitations. The Company, however, would owe KHK 30% of other, non-research and development payments it may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in up to five specified European Union ("EU") countries ("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 the Company earned in February 2018 upon EUSA's reimbursement approval from the NICE in the United Kingdom in first-line RCC was subject to the 30% KHK sublicense fee, or $0.6 million, which was paid in April 2018.

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 Topic 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 AVEO. 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. None of the remaining regulatory-related milestones have been included in the transaction price as these milestone amounts are 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 through April 2022.

Previously, under ASC 605, the $2.5 million in upfront consideration was being recognized over the Company's performance period from contract execution in December 2015 through the remaining patent life of tivozanib in April 2022 and, accordingly, did not represent a change under ASC 606.

Previously, under ASC 605, the Company recognized regulatory milestones when they were achieved. The $4.0 million research and development reimbursement payment upon marketing approval by the EMA in RCC in August 2017 was recognized as revenue in the third quarter of 2017 in accordance with ASC 605-28, Revenue Recognition—Milestone Method, as the underlying milestone was considered to be substantive and, accordingly, did represent a change under ASC 606. The impact of the adoption of ASC 606 on January 1, 2018 resulted in increases

of approximately $2.7 million in each of deferred revenue and the accumulated deficit. This amount represents the $4.0 million gross amount of the research and development reimbursement payment for marketing approval by the EMA in RCC, less the approximate $1.3 million that otherwise would have been recognized as collaboration and licensing revenue related to the cumulative catch-up for the period from contract execution in December 2015 through December 31, 2017, just prior to the adoption of ASC 606.

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. The commercial launch expanded to the United Kingdom following the reimbursement approval by the NICE in February 2018. In addition, EUSA has launched FOTIVDA in several non-EU5 European countries and is working toward launching FOTIVDA in additional European territories. The Company recognized approximately $132,000 and $275,000 in revenue for sales royalties in the three months and nine months ended September 30, 2018, 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. The Company recognized approximately $0.5 million and $4.1 million, respectively, in total revenues under the EUSA Agreement in the three months ended September 30, 2018 and 2017, respectively, and approximately $1.9 million and $4.3 million in the nine months ended September 30, 2018 and 2017, respectively. As of September 30, 2018, there was approximately $4.8 million in total deferred revenue that will continue to be recognized as collaboration and licensing revenue, in the approximate amount of $0.3 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 and nine months ended September 30, 2018 (in thousands):

Revenue Type	Date Achieved	Three Months Ended September 30, 2018	Nine Months Ended September 30, 2018
Collaboration and Licensing Revenue:			
Amounts in contract liabilities at the beginning of the period:			
Upfront payment	December 2015	$ 98	$ 296
R&D payment - EMA approval in RCC	August 2017	158	474
New amounts in contract liabilities during the current period:			
Milestone - UK reimbursement approval	February 2018	79	881
		$ 335	$ 1,651
Partnership Royalties		132	275
Total		$ 467	$ 1,926

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, 2018 (in thousands):

Contract Assets	Beginning Balance January 1, 2018	Additions	Deductions	Ending Balance September 30, 2018
Accounts Receivable	$18	$ 2,275	$ (2,161)	132

Contract Liabilities	Transaction	Date Paid	Deferred Revenue Beginning	Additions	Deductions	Ending

	Price	Date Achieved		Balance January 1, 2018			Balance September 30, 2018
Amounts in contract liabilities at the beginning of the period:							
Upfront payment	$ 2,500	December 2015	December 2015	$1,697	$ —	$ (296)	$ 1,401
R&D payment - EMA approval in RCC	4,000	August 2017	September 2017	2,711	—	(474)	2,237
New amounts in contract liabilities during the current period:							
Milestone - UK reimbursement approval	2,000	February 2018	March 2018	—	1,316	(198)	1,118
Total	$ 8,500			$4,408	$ 1,316	$ (968)	$ 4,756

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 $0.1 million and $0.6 million in the three months ended September 30, 2018 and 2017, respectively, and approximately $0.6 million in each of the nine months ended September 30, 2018 and 2017. As of September 30, 2018, the Company had recognized approximately $1.5 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 $0.5 million in prepaid cost sharing was classified as deferred research and development reimbursements as of September 30, 2018 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 the Novartis Agreement under which the Company granted to Novartis the exclusive right to develop and commercialize AV-380 and the Company's related antibodies worldwide. The Company also granted Novartis an option to purchase the Company's then-existing supply of AV-380 biological drug substance at an undiscounted price. Novartis was responsible under the Novartis Agreement for the development, manufacture and commercialization of AV-380 and any resulting approved therapeutic products.

On June 29, 2018, Novartis notified the Company that it would be terminating the Novartis Agreement without cause effective on August 28, 2018. Novartis' termination triggered the termination of all licenses and other rights granted by the Company to Novartis with regard to the AV-380 program, and the grant by Novartis to the Company of an irrevocable, exclusive, fully paid-up license, with a right to sub-license, to any patent rights or know-how controlled by Novartis as of the termination date related to the AV-380 program. Following termination, Novartis has initiated the process of transferring to the Company all preclinical, technical, manufacturing and other data developed by Novartis. The Company and Novartis are in discussions regarding other terms of the transfer of the AV-380 program back to the Company.

In connection with entry into the Novartis Agreement, Novartis made a non-refundable upfront payment to the Company of $15.0 million in September 2015. In December 2015, Novartis exercised an option to acquire the Company's inventory of clinical quality, AV-380 biological drug substance and reimbursed the Company approximately $3.5 million for such existing inventory. In February 2017, Novartis agreed to pay the Company $1.8 million out of its future payment obligations, if any, to the Company under the Novartis Agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that the Company owed to St. Vincent's Hospital Sydney Limited ("St. Vincent's") in March 2017. Under the Novartis Agreement, the Company had been eligible to receive milestone payments and royalties tied to the commencement of clinical trials, to regulatory approvals and to sales of such products upon commercialization. None of the milestones set forth in the Novartis Agreement had been achieved prior to the termination of the Novartis Agreement.

Accounting Analysis Under ASC 606

The Company evaluated the Novartis Agreement under ASC 606. Based on this evaluation, the Company identified the following promised goods and services at the inception of the Novartis Agreement: the Company's grant of an exclusive, worldwide license to develop and commercialize the Product, including all technical knowledge and data useful in the development and manufacture of the Product. The Company concluded the license and know-how were functional intellectual property. The Company concluded its promise to provide 90 days of transition assistance was immaterial in the context of the contract based on consideration of qualitative and quantitative factors. In making this evaluation the Company considered the specific personnel and time commitment that would be required to provide any transition services, concluding that the time commitment would be insignificant. The Company also concluded the option to purchase AV-380 drug substance did not represent a material right as the purchase price was undiscounted and thus did not represent a performance obligation but would instead be accounted for as a separate arrangement if and when the option was exercised. Accordingly, the Company determined at inception the agreement contained a single performance obligation related to the exclusive license to develop and commercialize AV-380 that was satisfied at the inception of the arrangement.

The Company determined that the $15.0 million in upfront consideration upon the execution of the Novartis Agreement in August 2015 and the $1.8 million payment in February 2017 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. None of the clinical, development and regulatory milestones have been included in the transaction price as these milestone amounts were fully constrained.

The Company evaluated Novartis' exercise of its option to purchase AV-380 drug substance in the fourth quarter of 2015 and identified a single performance obligation related to the delivery of AV-380 drug substance. The performance obligation was satisfied in connection with Novartis' exercise of its option and thus the Company recognized the total transaction price of $3.5 million at the time the option was exercised.

Previously, under ASC 605, the Company recognized the $15.0 million in upfront consideration as collaboration and licensing revenue in the third quarter of 2015 and the $1.8 million payment in February 2017 as collaboration and licensing revenue in

the first quarter of 2017 as these amounts were fixed, determinable and non-refundable, and there were no undelivered elements. Previously, under ASC 605, the Company recognized the $3.5 million purchase of the Company's inventory of clinical quality, AV-380 biological drug substance as collaboration and licensing revenue in the fourth quarter of 2015 upon the satisfaction of its performance obligation to deliver the AV-380 drug substance. Accordingly, as the timing and amount of revenue recognition for the payments received from Novartis are the same under ASC 605 and ASC 606, there was no transition adjustment required as of January 1, 2018.

Biodesix

In April 2014, the Company entered into a worldwide co-development and collaboration agreement with Biodesix (the "Biodesix Agreement") to develop and commercialize ficlatuzumab, the Company's HGF inhibitory antibody. 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 includes the right to sublicense, subject to certain exceptions. Pursuant to a joint development plan, the Company retains primary responsibility for clinical development of ficlatuzumab. In September 2016, the Company and Biodesix announced the termination of a phase 2 proof-of-concept clinical study of ficlatuzumab in which VeriStrat® was used to select clinical trial subjects (the "FOCAL" trial).

Under the Biodesix Agreement, with the exception of the costs incurred for the FOCAL trial, the Company and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab. Pursuant to the Biodesix Agreement, Biodesix was obligated to provide up to $15 million for the FOCAL trial, following which all costs of the FOCAL trial would be shared equally. In connection with the discontinuation of the FOCAL trial on October 14, 2016, the Company and Biodesix amended the Biodesix Agreement. Under the amendment, the Company agreed to share 50% of the shutdown costs for the FOCAL trial after August 1, 2016. In return for bearing these shutdown costs, the Company will be entitled to recover an agreed multiple of the additional costs borne by the Company out of any income Biodesix receives from the partnership in connection with the licensing or commercialization of ficlatuzumab. Following such recovery, the payment structure under the original Biodesix Agreement, which generally provides that the parties share equally in any costs and revenue, will resume without such modification.

In addition, the Company and Biodesix are funding investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer.

Pending marketing approval or the sublicense of ficlatuzumab, and subject to the negotiation of a commercialization agreement, each party would share equally in commercialization profits and losses, subject to the Company's right to be the lead commercialization party.

Prior to the first commercial sale of ficlatuzumab, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an "Opt-Out". If either AVEO or Biodesix elects to Opt-Out, with such party referred to as the "Opting-Out Party", then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. If AVEO elects to Opt-Out, it will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab. After election of an Opt-Out, the

non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances.

Prior to any Opt-Out, the parties shall share equally in any payments received from a third-party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third-party payments. The 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 Biodesix is an active participant in the ongoing development of ficlatuzumab via its participation on a joint steering committee that oversees the development plans for ficlatuzumab and is exposed to significant risk and rewards in connection with the activity based on its obligation 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 $26 thousand during the three months ended September 30, 2018 and 2017, respectively, and by approximately $0.3 million and $0.2 million in the nine months ended September 30, 2018 and 2017, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $0.1 million as of September 30, 2018.

Astellas Pharma

In February 2011, the Company, together with its wholly-owned subsidiary AVEO Pharma Limited, entered into a collaboration and license agreement (the "Astellas Agreement") with Astellas Pharma Inc. and certain of its subsidiaries (together, "Astellas"), pursuant to which the Company and Astellas intended to develop and commercialize tivozanib for the treatment of a broad range of cancers. Astellas elected to terminate the agreement effective on August 11, 2014, at which time the tivozanib rights were returned to the Company. In accordance with the Astellas Agreement, committed development costs, including the costs of completing certain tivozanib clinical development activities, continue to be shared equally.

The Company accounts for the joint development and commercialization activities in North America and Europe as a joint risk-sharing collaboration in accordance with ASC 808. Payments from Astellas with respect to Astellas' share of tivozanib development and commercialization costs incurred by the Company pursuant to the joint development plan, including the costs of completing certain tivozanib clinical development activities described in the preceding paragraph, were recorded as a reduction to research and development expense and general and administrative expense in the accompanying consolidated financial statements due to the joint risk-sharing nature of the activities in North America and Europe. The net amount due to the Company from Astellas pursuant to the cost-sharing provisions was $0.1 million at September 30, 2018.

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, 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, will generate data sufficient to support advancement to a phase 3 clinical trial.

In March 2014, the Company and Biogen amended the exclusive option and license 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 AVEO) 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, AVEO 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 AVEO 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 CNDA 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. The Company is required to make milestone payments, up to an aggregate total of $16.7 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 March 2017, as further described above under the heading "—Novartis," the Company paid a $1.8 million time-based milestone obligation that it owed to St. Vincent's and recognized $1.8 million in research and development expense. In January 2019, the Company will owe an additional $2.3 million time-based milestone obligation to St. Vincent's. 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 Hakko Kirin (KHK)

In December 2006, the Company entered into a license agreement with KHK ("KHK Agreement") under which it obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all potential indications. Its exclusive license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. Under the KHK Agreement, the Company obtained exclusive rights in its territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. The Company and KHK 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 KHK Agreement.

Under the KHK Agreement, the Company is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in its territory. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in its territory, neither the Company nor any of its subsidiaries has the right to conduct certain clinical trials of, seek marketing approval for or commercialize any other cancer product that also works by inhibiting the activity of a VEGF receptor.

The Company has upfront, milestone and royalty payment obligations to KHK under the KHK Agreement. Upon entering into the KHK Agreement, the Company made an upfront payment in the amount of $5.0 million. In March 2010, the Company made a milestone payment to KHK 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 KHK in connection with the acceptance by the FDA of the Company's 2012 NDA filing for tivozanib. Each milestone under the KHK Agreement is a one-time only payment obligation, accordingly, the Company did not owe KHK 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 KHK when the Company files its anticipated NDA with the FDA following the receipt of positive TIVO-3 topline data. If the Company obtains approval for tivozanib in the United States., the Company would owe KHK a one-time milestone payment of $18.0 million, provided that the Company does not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. If the Company were to sublicense the U.S. rights, the associated U.S. regulatory milestone would be replaced by a specified percentage of

sublicensing revenue, as set forth below.

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 KHK Agreement relating to rights the Company retains. The Company is required to pay KHK 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 approval from the European Commission of 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 KHK. 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 KHK, subject to certain limitations. The Company would, however, owe KHK 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 the Company earned in February 2018 upon EUSA's reimbursement approval from the NICE in the United Kingdom in first-line RCC was subject to the 30% KHK sublicense fee, or $0.6 million, which was paid in April 2018.

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.

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

(5) Other Accrued Liabilities

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

	September 30, 2018	December 31, 2017
Professional fees	$ 944	$ 844
Compensation and benefits	1,153	1,325
Other	1,093	289
Total	$ 3,190	$ 2,458

(6) Loans Payable

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 (the “2012 Amendment”), September 2014 (the “2014 Amendment”) and May 2016 (the “2016 Amendment”). Amounts borrowed under the 2012 Amendment were repaid in full in 2015. In December 2017, the Company entered an amended and restated loan and security agreement (the “2017 Loan Agreement”) with Hercules Funding III, LLC and Hercules Capital, Inc. (collectively “Hercules”).

Pursuant to the 2014 Amendment, the Company received additional loan proceeds from Hercules in the amount of $10.0 million and was required to make an end-of-term payment of approximately $0.5 million on January 1, 2018. This payment was made on the first business day of 2018. The Company incurred approximately $0.2 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount.

In connection with the 2014 Amendment, the Company issued warrants to the lenders to purchase up to 608,696 shares of the Company's common stock at an exercise price equal to $1.15 per share. The Company recorded the fair value of the warrants of approximately $0.4 million as stockholders' equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the loan using the effective interest method. In July 2017, Hercules exercised all 608,696 warrants. Pursuant to the terms of the warrant, Hercules, at their election, exercised the warrants via a non-cash "net share issuance." The Company issued Hercules 369,297 shares of its common stock and did not receive any cash proceeds in connection with the warrant exercise.

Pursuant to the 2016 Amendment, the Company received additional loan proceeds from Hercules, in an aggregate amount of $10.0 million, in installments of $5.0 million in each of May 2016 and June 2017, which increased the aggregate outstanding principal balance under the First Loan Agreement to $20.0 million. The Company is required to make an end-of-term payment totaling $0.3 million on December 1, 2019. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount. The 2016 Amendment included a financial covenant that required the Company to maintain an unrestricted cash position (defined as cash and liquid cash, including marketable securities) greater than or equal to $10.0 million through the date of completion of the Company's TIVO-3 trial, with results that were satisfactory to Hercules. Principal payments were scheduled to commence on January 1, 2018 and the loan was scheduled to mature on December 1, 2019.

In connection with the 2016 Amendment, the Company issued warrants to Hercules to purchase up to 1,202,117 shares of the Company's common stock at an exercise price equal to $0.87 per share. The Company recorded the fair value of the warrants of approximately $0.7 million as a component of stockholders' equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the loan using the effective interest method. In July 2017, Hercules exercised all 1,202,117 warrants. Pursuant to the terms of the warrant, Hercules, at their election, exercised the warrants via a non-cash "net share issuance." The Company issued Hercules 846,496 shares of its common stock and did not receive any cash proceeds in connection with the warrant exercise.

In connection with the 2016 Amendment, Hercules also received an option, subject to the Company's written consent, not to be unreasonably withheld, to purchase, either with cash or through conversion of outstanding principal under the loan, up to $2.0 million of equity of the Company sold in any sale by the Company to third parties of equity securities resulting in at least $10.0 million in net cash proceeds to the Company, subject to certain exceptions.

In connection with the Company's May 2016 private placement (refer to Note 7, "Common Stock – Private Placement / PIPE Warrants"), Hercules purchased 259,067 units for cash proceeds of $0.2 million to the Company. This purchase was separate from the $2.0 million equity purchase option under the 2016 Amendment. Each unit in the May 2016 private placement included one share of the Company's common stock and a PIPE Warrant to purchase one share of the Company's common stock at an exercise price of $1.00 per share. In July 2017, Hercules exercised its PIPE Warrants with respect to all 259,067 shares of common stock underlying such PIPE Warrants. The Company issued Hercules 259,067 shares of its common stock and received approximately $0.3 million in cash proceeds.

In December 2017, the Company entered into the 2017 Loan Agreement to refinance the Company's 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 new $20.0 million loan facility has 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, Hercules did not receive any additional warrants to purchase shares of the Company's common stock and no longer has the option, subject to the Company's written consent, to participate in its future equity financings up to $2.0 million through the purchase of the Company's common stock

either with cash or through the conversion of outstanding principal under the loan.

The loan maturity date has been revised from December 2019 to July 2021. The Company is not required to make principal payments until February 1, 2019, at which time the Company will be 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, which increases the total end-of-term payments under the 2014 Amendment, 2016 Amendment and 2017 Loan Agreement to approximately $1.6 million. The end-of-term payments under the 2014 Amendment, in the approximate amount of $0.5 million, and the 2016 Amendment, in the amount of $0.3 million, continue to be due on their original due dates of January 1, 2018 and December 1, 2019, respectively. 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 has been removed. Per the 2017 Loan Agreement, the interest rate decreased from 11.9% to 9.45%. The interest rate increased from 9.45% to 9.70% and from 9.70% to 9.95% in June 2018 and September 2018, respectively, due to the corresponding increases in the prime interest rates. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2017 Loan Agreement was accounted for as a loan modification in accordance with ASC 470-50.

The interest-only period could be extended by two 6-month deferrals upon the achievement of specified milestones relating to the development of tivozanib, including (i) on or prior to September 30, 2018, the Company has received positive data with respect to its TIVO-3 trial for the treatment of RCC for patients in the third-line setting which positive data supports the filing of an NDA with the FDA, subject to confirmation by Hercules at its reasonable discretion, and (ii) on or prior to June 28, 2019, the Company has received approval from the FDA for its tivozanib product for the treatment of RCC for patients in the third-line setting, subject to confirmation by Hercules at its reasonable discretion.

The unamortized discount to be recognized over the remainder of the loan period was approximately $1.1 million and $1.5 million as of September 30, 2018 and December 31, 2017, respectively.

The Company must make interest payments on the loan balance each month it remains outstanding. Per annum interest is payable on the principal balance of the loan each month it remains outstanding 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% (9.95% as of September 30, 2018).

The loans are secured by a lien on all the Company’s personal property (other than intellectual property), whether owned or acquired after the date of the First Loan Agreement. The 2017 Loan Agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company’s business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the 2017 Loan Agreement, the related liens or the priority thereof. As of September 30, 2018, 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 2017 Loan Agreement.

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 in current and long-term liabilities based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of September 30, 2018 are as follows (amounts in thousands):

Year Ending December 31:	
2018 (remaining 3 months)	$491
2019	8,755
2020	9,041
2021	6,104
	24,391
Less amount representing interest	(3,301)
Less unamortized discount	(1,123)
Less deferred charges	(1,090)
Less loans payable current, net of discount	(4,256)
Loans payable, net of current portion and discount	$14,621

(7) Common Stock

Settlement Warrants

On July 16, 2018, the Company issued and delivered 2.0 million Settlement Warrants to purchase shares of its common stock for a one-year period after the date of issuance at an exercise price equal to $3.00 per share. Refer to Note 3, “Significant Accounting Policies - Class Action Settlement and Settlement Warrants” for further discussion.

Sales Agreement with Leerink Capital Partners LLC

In February 2018, the Company entered into the Leerink Sales Agreement, 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 Leerink as its sales agent, with any sales of common stock through Leerink Capital Partners LLC (“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 Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. No shares of the Company’s common stock were sold under the Leerink Sales Agreement as of September 30, 2018.

In the fourth quarter of 2018 to-date, the Company sold 3,781,389 shares pursuant to the Leerink Sales Agreement, resulting in net proceeds of approximately $8.4 million, net of commissions.

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.

Public Offering – August 2018

On August 21, 2018, the Company closed an underwritten public offering of 2,500,000 shares of its common stock at the public offering price of $2.26 per share for gross proceeds of approximately $5.7 million. Two greater than 5% stockholders, including an entity affiliated with New Enterprise Associates and another stockholder purchased 2,000,000 shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to the Company were approximately $5.1 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

Public Offering – March 2017

On March 31, 2017, the Company closed an underwritten public offering of 34,500,000 shares of its common stock, including the exercise in full by the underwriter of its option to purchase 4,500,000 shares, at the public offering price of $0.50 per share for gross proceeds of approximately $17.3 million. Certain of the Company's executive officers and a director purchased an aggregate of 420,000 shares and an entity affiliated with New Enterprise Associates purchased 6,000,000 shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

Private Placement / PIPE Warrants

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 17,642,482 units, at a price of $0.965 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 $1.00 per share and are exercisable for a period of five years from the date of issuance. Certain of the Company's directors and executive officers purchased an aggregate of 544,039 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, 2018, PIPE Warrants exercisable for 777,201 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 16,865,281 shares of common stock were outstanding. In July 2017, Hercules exercised its PIPE Warrants with respect to all 259,067 shares of common stock underlying such PIPE Warrants, and the Company issued Hercules 259,067 shares of its common stock and received approximately $0.3 million in cash proceeds. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and the Company issued 518,134 shares of its common stock and received approximately $0.5 million in cash proceeds.

Sales Agreement with FBR

In February 2015, the Company entered into a sales agreement (the "FBR Sales Agreement") with FBR & Co. and MLV & Co. (together "FBR"), pursuant to which the Company could issue and sell shares of its common stock from time to

time up to an aggregate amount of $17.9 million, at the Company's option, through FBR as its sales agent, with any sales of common stock through FBR being made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act or in other transactions pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay FBR a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the FBR Sales Agreement.

In June 2017, the Company conducted its final transaction under the FBR Sales Agreement and sold approximately 6.5 million shares pursuant to the FBR Sales Agreement, as amended, resulting in proceeds of approximately $8.8 million, net of commissions and issuance costs. The FBR Sales Agreement has expired.

(8) Stock-based Compensation

Stock Incentive Plan

The Company maintains the 2010 Stock Incentive Plan (the "Plan") for employees, consultants, advisors, and directors, as amended in March 2013, June 2014 and June 2017. The Plan provides for the grant of equity awards such as stock options and restricted stock. In June 2017, the Company amended the Plan to increase the total number of shares reserved under the Plan by 3,500,000 from 8,500,000 shares to 12,000,000 shares. The amendment was adopted by the Board of Directors in February 2017 and approved by stockholders at the Annual Meeting of Stockholders held on June 21, 2017. The Plan provides 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 award 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. Options and restricted stock granted under the Plan vest over periods as determined by the Board, which generally are equal to four years. Options generally expire ten years from the date of grant. As of September 30, 2018, there were 1,019,906 shares of common stock available for future issuance under the Plan.

The following table summarizes stock option activity during the nine months ended September 30, 2018:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2018	7,537,958	$ 2.00		
Granted	2,635,115	3.04		
Exercised	(190,921)	1.16		
Forfeited	(104,308)	6.38		
Outstanding at September 30, 2018	9,877,844	$ 2.25	7.55	$14,405,000
Exercisable at September 30, 2018	4,845,673	$ 2.26	6.40	$9,044,000

Stock options to purchase 488,626 shares of common stock contain performance-based milestone conditions, which were not deemed probable of vesting at September 30, 2018.

The aggregate intrinsic value is based upon the Company's closing stock price of $3.31 on September 28, 2018, the last trading day of the quarter.

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. The Company did not grant any stock options in the three months ended September 30, 2018.

	Three Months Ended	
	September 30,	
	2018	2017
Volatility factor	—	79.03%
Expected term (in years)	—	6.25
Risk-free interest rates	—	2.06%
Dividend yield	—	—

	Nine Months Ended	
	September 30,	
	2018	2017
Volatility factor	80.18% - 83.40%	71.82% - 79.03%
Expected term (in years)	5.50 - 6.25	5.50 - 6.25
Risk-free interest rates	2.64% - 2.85%	1.84% - 2.10%
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.

The Company calculates volatility using its historical stock price data. Due to lack of available option activity data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the 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. Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the nine months ended September 30, 2018 and 2017 was $2.15 and $0.63, respectively.

On January 1, 2017, the Company adopted ASU No. 2016-09, Compensation–Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting and elected to account for forfeitures as they occur. Prior to 2017, the Company included an estimate of the value of the awards that would be forfeited in calculating compensation costs, which the Company estimated based upon actual historical forfeitures. The forfeiture estimates were recognized over the requisite service period of the awards on a straight-line basis.

As of September 30, 2018, there was $6.4 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 2.6 years.

(9) Legal Proceedings

In June 2018, the Company settled a consolidated class action lawsuit (the "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 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 "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 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 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 Class the Settlement Warrants, for the purchase of 2.0 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.

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. Refer to Note 3, “Significant Accounting Policies - Class Action Settlement and Settlement Warrants” for further discussion.

In 2013, the SEC also served a subpoena on the Company for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC invited the Company to discuss the settlement of potential claims asserting that the Company violated federal securities laws by omitting to disclose to investors the recommendation by the staff of the FDA on May 11, 2012, that the Company conduct an additional clinical trial with respect to tivozanib. On March 29, 2016, the SEC filed a complaint against the Company and three of its former officers in the District Court alleging that the Company misled investors about its efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the SEC’s complaint, the Company consented to the entry of a final judgment pursuant to which the Company paid the SEC a $4.0 million civil penalty to settle the SEC’s claims against it. As this settlement was probable and estimable as of December 31, 2015, the Company recorded an estimated settlement liability of $4.0 million and recorded a corresponding loss in the Statement of Operations as a component of operating expenses. On March 31, 2016, the District Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined the Company from violating Section 17(a) of the Securities Act of 1933, as amended, Sections 10(b) and 13(a) of the Exchange Act and rules 10b-5, 12b-20, 13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered the Company to pay the agreed-to civil penalty. On September 15, 2017 and October 31, 2017, respectively, two of the Company’s former officers consented to entry of final judgment to settle the SEC’s claims against them. The Company is not a party to the litigation between the SEC and the remaining former officer, and the Company can make no assurance regarding the outcome of that action or the SEC’s claims against that individual.

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," "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 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 a biopharmaceutical company dedicated to advancing a broad portfolio of targeted medicines for oncology and other areas of unmet medical need. Our strategy is to retain North American rights to our oncology portfolio while securing partners in development and commercialization outside of North America. We are working to develop and commercialize our lead candidate tivozanib in North America as a treatment for advanced or metastatic renal cell carcinoma, or RCC. On November 5, 2018, we announced positive topline results from the primary analysis of the Company's phase 3 trial of tivozanib in the third- and fourth-line treatment of patients with RCC, which we refer to as the TIVO-3 trial, a randomized, controlled, multi-center, open-label study to compare tivozanib to sorafenib (Nexavar®), an approved therapy, in 351 subjects with RCC. The TIVO-3 trial met its primary endpoint for progression-free survival, or PFS. The analysis of the secondary endpoint of overall survival, or OS, was not mature at the time of the final PFS analysis. Based on the results of the TIVO-3 trial, together with the previously completed phase 3 trial of tivozanib in the first line treatment of RCC, which we refer to as the TIVO-1 trial, we plan to submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or the FDA, within approximately six months from our announcement of topline data results of the TIVO-3 trial. We have outlicensed tivozanib (FOTIVDA®) for oncological indications in Europe and other territories outside of North America, and it is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with RCC and for adult patients who are vascular endothelial growth factor receptor and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. We have entered into partnerships to fund the development and commercialization of AV-203 and ficlatuzumab, both clinical stage assets in oncology. We are currently seeking a partner to develop our preclinical AV-353 platform in pulmonary arterial hypertension and oncology. In addition, a new formulation of tivozanib is being explored in ocular conditions. We have recently regained the rights to our AV-380 program for the potential treatment of cachexia and are considering a variety of options to advance the program's development.

Going Concern

We have identified conditions and events that raise 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. As of September 30, 2018, we had approximately $20.4 million in cash, cash equivalents and marketable securities. In the

fourth quarter of 2018 to-date, we sold approximately 3.8 million shares of our common stock pursuant to our sales agreement with Leerink Partners LLC, or the Leerink Sales Agreement, and received approximately $8.4 million in net proceeds. Based on these available cash resources, we do not have sufficient cash on hand to support current operations for at least the next 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. We expect that, in order to obtain additional funding, we will need to receive additional milestone payments and royalties from our partners and / or complete additional public or private financings of debt or equity. We may also seek to procure additional funds through future arrangements with collaborators, licensees or other third parties, and these arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates. Moreover, we may not be able receive milestone payments or complete financings or enter into such arrangements on acceptable terms, if at all. For more information, refer to "—Liquidity and Capital Resources—Operating Capital Requirements and Going Concern" below and Note 1, "—Liquidity and Going Concern" of the Notes to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Tivozanib

Our pipeline includes our lead candidate tivozanib, an oral, once-daily, vascular endothelial growth factor receptor tyrosine kinase inhibitor, or VEGFR TKI. Tivozanib is a potent, selective and long half-life inhibitor of all three VEGF receptors and is designed to optimize VEGF blockade while minimizing off-target toxicities, potentially resulting in improved efficacy and minimal dose modifications. Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal and breast cancers, as well as in age-related macular degeneration. We have exclusive rights to develop and commercialize tivozanib in all countries outside of Asia and the Middle East under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KHK. We have sublicensed to EUSA Pharma (UK) Limited, or EUSA, the right to develop and commercialize tivozanib in our licensed territories outside of North America, including Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa and Australasia. The EUSA sublicense excludes non-oncologic ocular conditions, to which we have retained development rights in all of our licensed territories.

Clinical and Regulatory Development in RCC

First-Line Phase 3 Trial (TIVO-1): We conducted the TIVO-1 trial, a global phase 3 clinical trial comparing the efficacy and safety of tivozanib with sorafenib, an approved therapy, for the first-line treatment of RCC. The trial met its primary endpoint for PFS with a median PFS in the tivozanib arm of 11.9 months compared with 9.1 months in the sorafenib arm. The trial also showed significant improvement in overall response rate, or ORR, of 33.1% for tivozanib versus 23.3% for sorafenib. The trial showed a favorable tolerability profile for tivozanib, as evidenced by fewer dose interruptions and dose reductions than sorafenib. However, the trial showed a non-statistically significant trend favoring the sorafenib treatment group in OS with a final median OS for the tivozanib treatment arm of 28.2 months and a final median OS for the sorafenib arm of 30.8 months (hazard ratio (HR) =1.245, p=0.105). We believe that an imbalance in subsequent therapy combined with the significant activity seen with tivozanib treatment following sorafenib contributed to the discordance in the efficacy results in the TIVO-1 trial between the PFS and ORR benefit, which significantly favored tivozanib, and the OS, which trended in favor of sorafenib.

In 2012, we submitted an NDA to the FDA seeking U.S. marketing approval for tivozanib. In June 2013, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from this single pivotal trial (TIVO-1), and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS.

TIVO-1 Extension Study - One-way crossover from sorafenib to tivozanib (Study 902): We completed a TIVO-1 extension study in which patients with RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib treatment arm in the TIVO-1 first-line RCC trial. We presented the results at the 2015 American Society of Clinical Oncology, or ASCO, Annual Meeting. In March 2018, long-term follow-up results from Study 902 were published in the European Journal of Cancer under the title “Efficacy of Tivozanib Treatment after Sorafenib in Patients with Advanced Renal Cell Carcinoma: Crossover of a Phase 3 Study,” reporting a median PFS of 11.0 month, a median OS of 21.6 months and an 18% ORR, further supporting the rationale for our current phase 3 TIVO-3 trial discussed below.

First-Line Approval in Europe: In February 2016 EUSA submitted an application for the use of tivozanib as a first-line treatment for RCC to the European Medicines Agency, or EMA, based on the data from our TIVO-1 clinical trial, as supported by data from the TIVO-1 extension trial, one phase 1 trial and two phase 2 trials in RCC. In June 2017, following an oral explanation, the Committee for Medicinal Products for Human Use, or CHMP, which is the scientific committee of the EMA, issued an opinion recommending tivozanib for approval. In August 2017, the European Commission approved tivozanib in all 28 countries of the European Union, Norway and Iceland. Tivozanib is sold under the brand name FOTIVDA, and is approved for the first-line treatment of adult patients with RCC and

for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC.

EUSA has commercially launched FOTIVDA in the United Kingdom, Germany, Austria, the Netherlands and Sweden. In November 2017, EUSA initiated product sales in Germany. In February 2018, EUSA commercially launched FOTIVDA in the United Kingdom upon receiving reimbursement approval from the United Kingdom's National Institute for Health and Care Excellence, or the NICE, for the first-line treatment of adult patients with RCC. In April 2018, FOTIVDA sales were also initiated in Austria. In July 2018, FOTIVDA received reimbursement approval in Scotland for the first-line treatment of adult patients with RCC. EUSA is working to secure reimbursement approval and commercially launch FOTIVDA in additional European countries.

Third-Line and Fourth-Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment in the TIVO-3 trial, a phase 3 trial of tivozanib in the third- and fourth-line treatment of patients with RCC. The TIVO-3 clinical trial was designed to address the FDA's concern about the negative OS trend expressed in the complete response letter from June 2013. TIVO-3 together with the previously completed TIVO-1 trial of tivozanib in the first line treatment of RCC, is designed to support a regulatory submission of tivozanib in the U.S. as a treatment for RCC in multiple lines of therapy. Our TIVO-3 trial design, which we reviewed with the FDA,

provides for a randomized, controlled, multi-center, open-label phase 3 clinical trial, with subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the trial must have failed two systemic therapies, including a VEGFR TKI. Patients may have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting the evolving treatment landscape. The primary objective of the TIVO-3 trial is to show improved PFS. Secondary endpoints include OS, safety and ORR. The trial's sites are located in North America and Europe. The TIVO-3 trial does not include a crossover design; accordingly, patients who progress in one therapy are not offered the opportunity to cross over to the other therapy.

The TIVO-3 trial enrolled a total of 351 patients. In October 2017, TIVO-3 successfully passed a pre-planned interim futility analysis. Based on the results of the futility analysis, which were reviewed by an independent statistician, the trial continued as planned without modification. The trial has also passed three semi-annual safety data assessments.

On November 5, 2018, we announced positive topline results from the primary analysis of the TIVO-3 trial. The trial met its primary endpoint for PFS, with a median PFS in the tivozanib arm of 5.6 months compared with 3.9 months in the sorafenib arm. Tivozanib demonstrated a 44% improvement in median PFS and 26% reduction in risk of progression or death compared to sorafenib (HR=0.74, p=0.02). Approximately 26% of patients received checkpoint inhibitor therapy in earlier lines of treatment, and PFS for tivozanib was longer than for sorafenib both in patients who received prior checkpoint inhibitor therapy and those who did not. The analysis of the secondary endpoint of OS was not mature at the time of the final PFS analysis, with only 46% of potential OS events having been reported. At the time of the preliminary OS analysis, no statistically significant difference in OS was observed (HR=1.06, p=0.69). The final OS analysis per protocol is planned for August 2019, two years following the date the last patient enrolled in the trial. In addition, we plan to present the totality of the data at medical meetings in 2019, and to the extent there is any meaningful change in OS at the time of such meetings, we would present those updated data. The secondary endpoint of ORR for patients receiving tivozanib was 18% compared to 8% for patients receiving sorafenib (p=0.02). Tivozanib was generally well-tolerated, with Grade 3 or higher adverse events consistent with those observed in previous tivozanib trials. 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.

Based on the results of the TIVO-3 trial, together with the previously completed TIVO-1 trial, we plan to submit an NDA to the FDA within approximately six months from our announcement of topline data results of the TIVO-3 trial.

RCC PD-1 Combination Trial with Opdivo® (TiNivo): In recent clinical trials, VEGFR TKI and immune checkpoint (PD-1) inhibitor combinations have shown promising efficacy in treating RCC. However, several combinations of non-specific VEGFR TKIs with anti-PD-1 antibodies have encountered toxicity levels that we believe have challenged or prohibited such VEGFR TKIs from safely combining with PD-1 inhibitors for RCC treatment, or required them to combine at reduced doses, which can potentially reduce efficacy. In our clinical trials, tivozanib has demonstrated lower rates of key potential overlapping toxicities with PD-1 inhibitors. Based on this data, we believe that tivozanib's tolerability profile may allow tivozanib to combine with PD-1 inhibitors with improved tolerability relative to other TKI plus PD-1 combinations reported to date.

In March 2017, we initiated enrollment in a phase 1b/2 clinical trial of tivozanib in combination with Opdivo (nivolumab), an immune checkpoint (PD-1) inhibitor, for the treatment of RCC, which we refer to as the TiNivo trial. The TiNivo trial enrolled a total of 28 patients. We are sponsoring the trial, for which Bristol-Myers Squibb, or BMS, has supplied nivolumab. The TiNivo trial is being led by the Institut Gustave Roussy in Paris under the direction of Professor Bernard Escudier, MD, Chairman of the Genitourinary Oncology Committee. The phase 1b portion of the TiNivo trial enrolled six patients. In June 2017, we successfully completed the phase 1 dose escalation portion of the trial, where oral tivozanib was administered in two escalating dose cohorts in combination with intravenous nivolumab at a constant 240 mg every two weeks. The full dose tivozanib regimen of 1.5 mg daily for 21 days,

followed by a 7-day rest period, was selected as the recommended phase 2 dose for the expansion portion of the trial. On November 3, 2017, the results from the phase 1b portion of the TiNivo trial were presented at the 16th International Kidney Cancer Symposium of the Kidney Cancer Association. The phase 1b portion of the TiNivo trial demonstrated that the combination of tivozanib and nivolumab was well tolerated to the full dose and schedule of single agent tivozanib, with no dose limiting toxicities.

The phase 2 portion of the trial, which enrolled an additional 22 patients, was designed to assess the safety, tolerability, and anti-tumor activity of the combination of tivozanib and nivolumab. On February 10, 2018, we presented preliminary results from the phase 2 portion of the TiNivo trial at the 2018 ASCO Genitourinary Cancers Symposium. On October 22, 2018, we presented updated interim results from all 25 patients treated at full dose at the ESMO 2018 Congress. The combination was generally well tolerated. Treatment-related Grade 3/4 adverse events occurred in 60% of patients, the most common of which was hypertension. Preliminary efficacy was assessed in all 25 patients, who were treated with the full dose and schedule of oral tivozanib in combination with intravenous nivolumab. Of these patients, 13 (52%) had received at least one prior systemic therapy, including 2 (8%) that had received prior PD-1 therapy, and 12 (48%) were treatment naïve. An ORR was observed in 14 patients (56%) (complete response plus partial response), including 1 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%). The 2 patients (8%) who received prior PD-1 therapy both achieved a partial response. At the time of data collection, 13 patients (52%) remained on study and 18 patients (72%) had tumor shrinkage of at least 25%, with a majority of patients having disease control for at least 48 weeks.

We are planning further development of tivozanib as a combination therapy with immune checkpoint inhibitors.

Clinical Development in HCC

NCCN-AVEO Phase 1b/2 Trial. In January 2018, Dr. Renuka Iyer from the Roswell Park Cancer Institute presented data at the 2018 ASCO Gastrointestinal Cancers Symposium from a multicenter, investigator-sponsored phase 1b/2 trial of tivozanib in previously untreated patients with advanced, unresectable hepatocellular carcinoma, or HCC. The trial was one of several studies funded by a grant we provided to the National Comprehensive Cancer Network.

The trial was designed to evaluate the safety and efficacy of tivozanib in advanced HCC, and enrolled a total of 21 patients at three trial sites. In the phase 1b portion of the trial, which used a modified 3 + 3 dose escalation design, 8 patients were dosed with tivozanib starting at 1.0 mg or 1.5 mg daily for 21 days followed by 7 days off drug. No dose-limiting toxicities were seen in cycle one in patients treated with 1.0 mg, and tivozanib at 1.0 mg daily was selected for the phase 2 expansion portion of the trial.

Of 19 evaluable patients in the trial, at a median follow up of 16.9 months, the trial's primary endpoint of median PFS and PFS at week 24 were 5.5 months and 47%, respectively. A partial response was seen in 4 of 19 patients (21%) and stable disease in 8 of 19 patients (42%), for a disease control rate of 63%. OS at 6 and 12 months was 58% and 25%, respectively, with a median OS of 7.5 months. As of the date of the presentation, four patients had maintained stable disease for over two years. There were no significant changes in hepatitis B or hepatitis C viral load during study treatment. Tivozanib was generally well tolerated at 1.0 mg daily, with adverse events consistent with those observed in previous tivozanib trials.

Following these trial results, we plan to explore potential development opportunities of tivozanib in HCC, both as a monotherapy and as a combination therapy.

Ficlatuzumab

Ficlatuzumab is a potent Hepatocyte Growth Factor, or 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 partnered with Biodesix, Inc., or Biodesix, under a worldwide Co-Development and Collaboration Agreement, or the Biodesix Agreement, to develop and commercialize ficlatuzumab. Under the Biodesix Agreement, we and Biodesix each contribute half of the development costs of ficlatuzumab.

Development in HNSCC. We and Biodesix funded an investigator-sponsored phase 1 clinical trial of ficlatuzumab in combination with cetuximab in squamous cell carcinoma of the head and neck, or HNSCC. In June 2017, preliminary results from the phase 1 trial were presented at the 2017 ASCO Annual Meeting. The trial of ficlatuzumab in combination with the EGFR inhibitor cetuximab in patients with cetuximab-resistant, metastatic HNSCC demonstrated activity with an overall response rate of 17% (two partial responses out of twelve patients), a disease control rate of 67% and prolonged PFS and OS compared to historical controls, in addition to being well tolerated. A randomized, phase 2, multicenter, investigator-initiated trial in ERBITUX® (cetuximab) refractory patients to confirm these findings was initiated in the fourth quarter of 2017 under the direction of Julie E. Bauman, MD, MPH, Chief, Division of Hematology/Oncology at the University of Arizona Cancer Center. The phase 2 trial is expected to enroll approximately 60 patients randomized to receive either ficlatuzumab alone or ficlatuzumab and cetuximab.

Development in AML. We and Biodesix are funding an investigator-sponsored phase 1/2 clinical trial of ficlatuzumab in combination with cytarabine in acute myeloid leukemia, or AML. In June 2017, preliminary results from the phase 1 trial were presented at the 2017 ASCO Annual Meeting. This trial, exploring ficlatuzumab in combination with high-dose cytarabine in patients

with high risk relapsed or refractory AML, demonstrated early signs of tolerability and activity, including a 50% complete response rate in the eight evaluable patients. The phase 2 portion is ongoing and expected to enroll ten additional patients.

Development in pancreatic cancer. We and Biodesix are funding an investigator-sponsored phase 1/2 clinical trial of ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer. The trial was initiated in December 2017 to test the safety and tolerability of ficlatuzumab when combined with nab-paclitaxel and gemcitabine in previously untreated metastatic pancreatic ductal cancer, or PDAC. Preclinical findings demonstrated a beneficial effect of the drug combination of ficlatuzumab and gemcitabine compared to either drug alone in an in-vivo model of PDAC. The goal of the trial is designed to determine maximum tolerated dose of ficlatuzumab when combined with gemcitabine and nab-paclitaxel. Secondary outcome measures include response rate and PFS. The trial, which is being conducted under the direction of Kimberly Perez, M.D. at the Dana-Farber Cancer Institute, is expected to enroll approximately 30 patients.

We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab. The expansion of the ficlatuzumab clinical program, beyond what we are committed to, would require additional manufacturing efforts and costs.

AV-203

AV-203 is a potent anti-ErbB3 (also known as HER3) specific monoclonal antibody with high ErbB3 affinity. We have observed potent anti-tumor activity in mouse models. AV-203 selectively inhibits the activity of the ErbB3 receptor, and our preclinical studies suggest that neuregulin-1 (also known as heregulin), or NRG1, levels predict AV-203 anti-tumor activity. We have completed a phase 1 dose escalation trial of AV-203, which established a recommended phase 2 dose, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy.

We have partnered with CANbridge Life Sciences Ltd., or CANbridge, to develop, manufacture and commercialize AV-203 in all countries outside of North America. We have retained the North American rights to AV-203. CANbridge's obligations include conducting and funding clinical development of AV-203 through phase 2 proof-of-concept in esophageal squamous cell carcinoma, or ESCC. Following proof-of-concept, we may decide to participate in later-stage worldwide development efforts. In December 2017, CANbridge filed an initial new drug application, or IND, in China seeking regulatory authorization to initiate clinical trials of AV-203, which CANbridge refers to as CAN017, in ESCC. In August 2018, the China National Drug Administration, or CNDA, approved this IND application. CANbridge has advised us that it expects that AV-203 will reenter the clinic in 2019.

AV-380

AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiation factor 15, or GDF15, a divergent member of the TGF-ß family, 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. Cachexia is associated with various cancers as well as chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, or COPD, anorexia nervosa and other diseases. AV-380 focuses on a significant area of unmet patient need. 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). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000

patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (Am J Clin Nutr 2006).

We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome. We have established preclinical proof-of-concept for GDF15 as a key driver of cachexia by demonstrating, in animal models, that the administration of GDF15 induces cachexia, and that inhibition of GDF15 reverses cachexia and provides a potential indication of an OS benefit. We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development. In connection with the AV-380 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.

In August 2015, we granted Novartis International Pharmaceutical Ltd., or Novartis, the exclusive right to develop and commercialize AV-380 and our related antibodies worldwide. On June 29, 2018, Novartis notified us that it would be terminating our collaboration without cause. Effective August 28, 2018, we regained the rights to AV-380 and are considering a variety of options to advance the program's development.

AV-353 Platform

The AV-353 platform includes a number of potent inhibitory antibody candidates 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 and neurodegenerative conditions. Publications, including Nature Medicine (2009), have implicated the Notch 3 pathway in PAH, a rare and life-threatening disorder that affects approximately 250,000 people worldwide (Global Data 2016 PAH Opportunity Analyzer; 2012 Decision Resources PAH Report) and is caused by thickening of the arterial walls in small arteries between the heart and the lungs, resulting in restricted blood flow. Currently, no known cure for PAH exists. Existing treatments for PAH have focused on controlling symptoms by avoiding vasoconstriction and increasing vasodilation of blood vessels but have not reversed the underlying cause of the disease. However, the results of a preclinical research study conducted at the University of California at San Diego and presented in a poster at the November 2016 American Heart Association meeting using one of our anti-Notch3 antibody candidates generated preclinical data that supports the ability of the antibody to potentially reverse the thickening of vascular smooth muscle cells, which would represent a disease-modifying approach to treatment. We are currently seeking a partner to develop the AV-353 platform worldwide for the potential treatment of PAH.

Strategic Partnerships

CANbridge

In March 2016, we entered into a collaboration and license agreement with CANbridge, or the CANbridge Agreement, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, our proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in all countries outside of North America. In addition, CANbridge has a right of first negotiation if we determine to outlicense 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. CANbridge has responsibility for all activities and costs associated with the development, manufacture and commercialization of AV-203 in its territories. CANbridge is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain and Germany. Under the CANbridge Agreement, CANbridge is required to conduct and fund the clinical development of AV-203 through phase 2 proof-of-concept in esophageal squamous cell carcinoma, or ESCC, after which we may elect to contribute to certain worldwide development efforts.

In December 2017, CANbridge filed an IND application with the CNDA for a clinical study of AV-203 in ESCC. CANbridge's IND application was accepted by the CNDA in August 2018. CANbridge has advised us that it plans to initiate a phase 1b/extension trial in ESCC in 2019.

Upon entry into the CANbridge Agreement, CANbridge paid us an upfront fee of $1.0 million in April 2016, net of foreign withholding taxes. CANbridge also reimbursed us for $1.0 million in certain AV-203 manufacturing costs that we previously incurred. 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 August 2018, CANbridge obtained regulatory approval of their IND application from the CNDA for a clinical study of AV-203 in ESCC and, accordingly, we earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018.

Pursuant to the CANbridge Agreement, we are 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, we are 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 or ten years after the first commercial sale of such licensed product in such country. A percentage of any milestone and royalty payments received by us under the CANbridge Agreement, excluding upfront and reimbursement payments, are due to Biogen Idec International GmbH, or Biogen, as a sublicensing fee under our option and license agreement with Biogen dated March 18, 2009, as amended. The $2.0 million development and regulatory milestone we earned in August 2018 for regulatory approval from the CNDA 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.

The term of the CANbridge Agreement continues until the last to expire royalty term applicable to licensed products. Either party may terminate the CANbridge Agreement in the event of a material breach of the CANbridge Agreement by the other party that remains uncured for a period of 45 days, in the case of a material breach of a payment obligation, and 90 days in the case of any other material breach. CANbridge may terminate the CANbridge Agreement without cause at any time upon 180 days' prior written notice to us. We may terminate the CANbridge Agreement upon thirty days' prior written notice if CANbridge challenges any of the patent rights licensed to CANbridge under the CANbridge Agreement.

EUSA

In December 2015, we entered into a license agreement with EUSA, or the EUSA Agreement, under which we 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 for all diseases and conditions in humans, excluding non-oncologic ocular conditions. EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout its licensed territories for RCC. EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in its licensed territories.

EUSA made research and development reimbursement payments to us of $2.5 million upon the execution of the EUSA Agreement in 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 TiNivo trial. 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 its territories. EUSA made an additional research and development reimbursement payment to us of $2.0 million upon its exercise of its opt-in right. This 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. We are also eligible to receive an additional research and development reimbursement payment from EUSA of 50% of our total costs for our TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that study.

We are entitled to receive milestone payments of $2.0 million per country upon reimbursement approval, if any, for RCC in each of France, Germany, Italy, Spain and the United Kingdom, which we refer to collectively as the EU5, and an additional $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the European Union, as mutually agreed by the parties. In February 2018, EUSA obtained reimbursement approval from the NICE in the United Kingdom for the first-line treatment of RCC. Accordingly, we earned a $2.0 million milestone payment that was received from EUSA in March 2018. We are 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 up to $335.0 million upon EUSA's achievement of certain sales thresholds. Upon commercialization, we are eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in its licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. In November 2017, we began earning sales royalties upon EUSA's commencement of the first commercial launch of tivozanib (FOTIVDA) with the initiation of product sales in Germany. The commercial launch expanded to the United Kingdom following the reimbursement approval by the NICE in February 2018. In addition, EUSA has launched FOTIVDA in several non-EU5 European countries and is working toward launching FOTIVDA in additional European territories. We recognized approximately $132,000 and $275,000 in revenue for sales royalties in the three months and nine months ended September 30, 2018, respectively.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to the EUSA Agreement, including any 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 we earned in February 2018 upon EUSA's reimbursement approval for FOTIVDA in the United Kingdom

was subject to the 30% KHK sublicense fee, or $0.6 million, which was paid in April 2018.

The term of the EUSA Agreement continues on a product-by-product and country-by-country basis until the later to occur of (a) the expiration of the last valid patent claim for such product in such country, (b) the expiration of market or regulatory data exclusivity for such product in such country or (c) the tenth anniversary of the effective date. Either party may terminate the EUSA Agreement in the event of the bankruptcy of the other party or a material breach by the other party that remains uncured, following receipt of written notice of such breach, for a period of (a) thirty (30) days in the case of breach for nonpayment of any amount due under the EUSA Agreement, and (b) ninety (90) days in the case of any other material breach. EUSA may terminate the EUSA Agreement at any time upon one hundred eighty (180) days' prior written notice. In addition, we may terminate the EUSA Agreement upon thirty (30) days' prior written notice if EUSA challenges any of the patent rights licensed under the EUSA Agreement.

Novartis

In August 2015, we entered into a license agreement with Novartis, or the Novartis Agreement, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies worldwide. Novartis was responsible

under the Novartis Agreement for the development, manufacture and commercialization of our antibodies and any resulting approved therapeutic products.

On June 29, 2018, Novartis notified us that it would be terminating our collaboration without cause. Effective August 28, 2018 we regained the rights to AV-380. We had been eligible to receive milestone payments and royalties tied to the commencement of clinical trials, to regulatory approvals and to sales of such products upon commercialization. We have not included any of the potential milestone or other potential payments to us under the Novartis Agreement in our cash forecasts. Accordingly, termination of the Novartis Agreement will not impact our cash guidance.

Novartis' termination without cause triggered the termination of all licenses and other rights granted by us to Novartis with regard to the AV-380 program, and the grant by Novartis to us of an irrevocable, exclusive, fully paid-up license, with a right to sub-license, to any patent rights or know-how controlled by Novartis as of the termination date related to the AV-380 program. Following termination, Novartis has initiated the process of transferring to us all preclinical, technical, manufacturing and other data developed by Novartis. We and Novartis are in discussions regarding other terms of the return of the AV-380 program.

Biodesix

In April 2014, we entered into a worldwide co-development and collaboration agreement with Biodesix, or the Biodesix Agreement, to develop and commercialize ficlatuzumab. Under the Biodesix Agreement, we and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab, and would share equally in any future revenue from development or commercialization, subject to certain exceptions. We retain primary responsibility for clinical development of ficlatuzumab, although all trials are conducted pursuant to a joint development plan.

Under the Biodesix Agreement, we 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 us 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 includes the right to sublicense, subject to certain exceptions. In October 2016, we amended the Biodesix agreement in connection with the termination of the FOCAL trial, a phase 2 proof-of-concept clinical study of ficlatuzumab in which VeriStrat was used to select clinical trial subjects.

Prior to the first commercial sale of ficlatuzumab, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an "Opt-Out". If either we or Biodesix elects to Opt-Out, with such party referred to as the "Opting-Out Party," then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. If we elect to Opt-Out, we will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab. After election of an Opt-Out, the non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances. Prior to any Opt-Out, the parties shall share equally in any payments received from a third-party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third-party payments. The Biodesix Agreement remains in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

We and Biodesix are currently funding several investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer. We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab. Such clinical development, beyond what we are committed to, would require additional manufacturing efforts and costs.

St. Vincent's Hospital

In July 2012, we entered into a license agreement with St. Vincent's, or the St. Vincent's Agreement, under which we obtained an exclusive, worldwide sublicensable right to develop, manufacture and commercialize products for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which is also known as GDF15. We believe GDF15 is a novel target for cachexia, and we are exploiting this license in our AV-380 program for cachexia. Under the St. Vincent's Agreement, we have non-exclusive rights to certain related diagnostic products and research tools and also have a right of first negotiation to obtain an exclusive license to certain improvements that St. Vincent's or third parties may make to licensed therapeutic products. We are obligated to use

diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product.

In 2012, we paid St. Vincent's an upfront license fee of $0.7 million. In August 2015, in connection with the execution of the Novartis Agreement, we amended and restated the St. Vincent's Agreement and paid St. Vincent's an additional upfront fee of $1.5 million. We are required to make milestone payments, up to an aggregate total of $16.7 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 we grant any sublicense, depending on the sublicensed territory. In March 2017, as further described above under the heading "—Novartis," we paid a $1.8 million time-based milestone obligation that we owed to St. Vincent's. We will owe an additional $2.3 million time-based milestone obligation to St. Vincent's in March 2019. In addition, we will be required to pay St. Vincent's tiered royalty payments equal to a low-single-digit percentage of any net sales we or our 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. Our royalty payment obligations for a licensed therapeutic product in a particular country end on the later of 10 years after the date of first commercial sale of such licensed therapeutic product in such country or expiration of the last-to-expire

valid claim of the licensed patents covering such licensed therapeutic product in such country and are subject to offsets under certain circumstances.

The St. Vincent's Agreement remains in effect until the later of 10 years after the date of first commercial sale of licensed therapeutic products in the last country in which a commercial sale is made, or expiration of the last-to-expire valid claim of the licensed patents, unless we elect, or St. Vincent's elects, to terminate the St. Vincent's Agreement earlier. We have the right to terminate the St. Vincent's Agreement on six months' notice if we terminate our GDF15 research and development programs as a result of the failure of a licensed therapeutic product in preclinical or clinical development, or if we form the reasonable view that further GDF15 research and development is not commercially viable, and we are not then in breach of any of our obligations under the St. Vincent's Agreement.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans outside of North America. In March 2014, we amended our agreement with Biogen Idec, and regained worldwide rights to AV-203. Pursuant to the amendment, we were obligated to in good faith use reasonable efforts to seek a collaboration partner to fund further development and commercialization of ErbB3-targeted antibodies. We satisfied this obligation in March 2016 upon entering into our CANbridge Agreement. We are obligated to pay Biogen Idec a percentage of milestone payments we receive under the CANbridge Agreement and single-digit royalty payments on net sales related to the sale of AV-203, up to cumulative maximum amount of $50.0 million.

The $2.0 million development and regulatory milestone we earned in August 2018 in connection with CANbridge's regulatory approval from the CNDA 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.

Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with KHK, or the KHK Agreement, under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all potential indications. Our exclusive license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. Under the KHK Agreement, we obtained exclusive rights in our territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. We and KHK 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 KHK Agreement.

Under the KHK Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in our territory, neither we nor any of our subsidiaries has the right to conduct certain clinical trials of, seek marketing approval for or commercialize any other cancer product that also works by inhibiting the activity of a VEGF receptor.

We have upfront, milestone and royalty payment obligations payable to KHK under our KHK Agreement. Upon entering into the KHK Agreement, we made an upfront payment in the amount of $5.0 million. In March 2010, we

made a milestone payment to KHK in the amount of $10.0 million in connection with the dosing of the first patient in TIVO-1, our first phase 3 clinical trial of tivozanib. In December 2012, we made a $12.0 million milestone payment to KHK in connection with the acceptance by the FDA of our 2012 NDA filing for tivozanib. Each milestone under the KHK Agreement is a one-time only payment obligation. Accordingly, we did not owe KHK another milestone payment in connection with the dosing of the first patient in our TIVO-3 trial and would not owe a milestone payment to KHK when we file our anticipated NDA with the FDA following the receipt of positive TIVO-3 topline data. If we obtain approval for tivozanib in the U.S., we would owe KHK a one-time milestone payment of $18.0 million, provided that we do not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. If we were to sublicense the U.S. rights, the associated U.S. regulatory milestone would be replaced by a specified percentage of sublicensing revenue, as set forth below.

If we sublicense any of our rights to tivozanib to a third party, as we have done with EUSA pursuant to the EUSA Agreement, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under our KHK Agreement relating to rights we retain. We are required to pay KHK a fixed 30% of amounts we

receive from our sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts we receive 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 in September 2017 upon the approval from the European Commission of tivozanib (FOTIVDA) and the $2.0 million upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial were not subject to sublicense revenue payments to KHK. 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 KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we 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 we earned in February 2018 upon EUSA's reimbursement approval for FOTIVDA in the United Kingdom as a first-line treatment for RCC was subject to the 30% KHK sublicense fee, or $0.6 million, which was paid in April 2018.

We are also required to pay tiered royalty payments on net sales we make of tivozanib in our 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. Our royalty payment obligations in a particular country in our 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.

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

Financial Overview

We do not have a history of being profitable and, as of September 30, 2018, we had an accumulated deficit of $616.8 million. We anticipate that we will continue to incur significant operating costs over the next several years as we continue our planned development activities for our preclinical and clinical products. We will need additional funding to support our operating activities, and the timing and nature of activities contemplated for 2019 and thereafter will be conducted subject to the availability of sufficient financial resources. Refer to the "—Going Concern" and "Liquidity and Capital Resources—Operating Capital Requirements and Going Concern" sections for a further discussion of our funding requirements.

Revenue

On January 1, 2018, we adopted the provisions of Accounting Standards Codification Topic 606, Revenue From Contracts with Customers, or ASC 606. Refer to Note 3, "Significant Accounting Policies - Revenue Recognition" and Note 4, "Collaborations and License Agreements", to our condensed consolidated financial statements included elsewhere in this Quarterly Form 10-Q for further information.

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) with the initiation of product sales in Germany. To date, these sales royalties are the only revenue we have generated from product sales.

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. We expect that any revenue we generate will fluctuate from quarter to quarter 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. We do not expect to generate revenue from product sales in the near term. 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 and stock-based compensation expense;
- external development-related expenses, including clinical trials conducted by contract research organizations and investigative sites, preclinical studies and consultants;
- the cost of acquiring and manufacturing drug development related materials and related distribution;
- costs associated with outsourced development activities, including regulatory and medical affairs;
- sublicense fees for, and milestone payments related to, in-licensed products and technology; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets.

Research and development expenses are net of amounts reimbursed under our agreements with EUSA, Biodesix, and Astellas 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 continue to decrease during the remainder of 2018 as we seek to complete the TIVO-3 and TiNivo trials. This estimate excludes possible additional Company-sponsored clinical trials and any related drug manufacturing and drug supply distribution, and pre-commercialization activities that we may undertake following the positive topline results from the primary analysis of the TIVO-3 trial that we announced on November 5, 2018, 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 quality of the product candidate’s early clinical data, 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.

General and Administrative Expenses

General and administrative expenses consist principally of salaries, bonuses and related costs for personnel in executive, finance, corporate development, information technology, legal and human resource functions. Other general and administrative expenses include facility costs not otherwise included in research and development expenses, patent filing, prosecution and defense costs and professional fees for legal, consulting, auditing and tax services. We anticipate that our general and administrative expenses will remain at current levels during the remainder of 2018, excluding pre-commercialization activities that we may undertake following the positive topline results from the primary analysis of the TIVO-3 trial that we announced on November 5, 2018, 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 17,642,482 shares of our common stock in connection with a private placement financing, which we refer to herein as the PIPE Warrants. 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, for a further discussion.

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.

As of September 30, 2018, PIPE Warrants exercisable for 777,201 shares of common stock had been exercised, for cash proceeds of approximately $0.8 million, and PIPE Warrants exercisable for 16,865,281 shares of common stock were outstanding. In July 2017, we issued to Hercules Capital Inc., or Hercules, 259,067 shares of common stock upon its exercise of all of its PIPE Warrants, and we received approximately $0.3 million in cash proceeds. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and we issued 518,134 shares of our common stock and received approximately $0.5 million in cash proceeds.

48

We recorded non-cash losses of approximately $16.2 million and $6.5 million in the three months and nine months ended September 30, 2018, respectively, and non-cash losses of approximately $23.5 million and $47.9 million in the three months and nine months ended September 30, 2017, respectively, in our Statement of Operations attributable to the increases in the fair value of the warrant liability that resulted from higher stock prices as of September 30, 2018 and September 30, 2017, relative to prior periods. In the nine months ended September 30, 2018, we recorded a reduction in the PIPE Warrant liability, with a corresponding increase to additional paid-in capital, of approximately $1.1 million attributable to PIPE Warrant exercises in the first quarter of 2018.

The key assumptions used to value the PIPE Warrants were as follows:

	Issuance	December 31, 2017	March 31, 2018	June 30, 2018	September 30, 2018
Expected price volatility	76.25%	84.86%	85.61%	78.27%	78.56%
Expected term (in years)	5.00	3.50	3.25	3.00	2.75
Risk-free interest rates	1.22%	2.09%	2.39%	2.63%	2.88%
Stock price	$ 0.89	$ 2.79	$ 2.90	$ 2.26	$ 3.31
Dividend yield	—	—	—	—	—

Class Action Settlement and Settlement Warrants

In December 2017, we entered into a binding memorandum of understanding, or MOU, to settle a securities class action lawsuit, or the Class Action, captioned In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, filed in 2013 in the United States District Court for the District of Massachusetts, or the District Court, against us and certain of our former officers. The Class Action was purportedly brought on behalf of stockholders who purchased our common stock between May 16, 2012 and May 1, 2013, or the Class.

Upon entry into the MOU, our liability related to this settlement became estimable and probable. Accordingly, we recorded an estimated $17.1 million contingent liability, including (a) $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 our insurance carriers, and (b) an approximate $2.1 million estimate for the fair value on December 31, 2017 of 2.0 million warrants to purchase shares of our common stock, or the Settlement Warrants, that we agreed to issue to the Class, with a corresponding non-cash charge to the Statement of Operations as a component of operating expenses. The Settlement Warrants are exercisable for a one-year period from their date of issue at an exercise price equal to $3.00 per share, which was the closing price on December 22, 2017, the trading day prior to the execution of the MOU.

In January 2018, we entered into a definitive stipulation of settlement agreement, or the Stipulation. In February 2018, the District Court preliminarily approved the Stipulation, following which the insurance carriers funded the settlement

escrow account related to the $15.0 million cash portion of the settlement. On May 30, 2018, the District Court approved the Stipulation in its order of final approval and final judgment, or the Final Judgment.

The settlement became effective on June 29, 2018, or the Effective Date, which was the date on which all of the following conditions had been met: (a) a Final Judgment containing the requisite release of claims had been entered by the District Court; (b) no appeal was pending with respect to the Final Judgment; (c) the Final Judgment had not been reversed, modified, vacated or amended; (d) the time to file any appeal from the Final Judgment had expired without the filing of an appeal or an order dismissing the appeal or affirming the Final Judgment had been entered, and any time to file a further appeal (including a writ of certiorari or for reconsideration of the appeal) had expired; and (e) the MOU and any settlement agreement with respect to the claims released in the Final Judgment had not expired or been terminated. Pursuant to the Final Judgment, all claims against us were released upon the Effective Date. In addition, pursuant to the Stipulation, we have no interest in the settlement escrow account subsequent to the Effective Date. Accordingly, the $15.0 million contingent liability associated with the cash portion of the settlement and the corresponding insurance recovery were eliminated on the Effective Date. We had agreed to use our best efforts to issue and deliver the Settlement Warrants within ten business days following the Effective Date. On July 16, 2018, we 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.

The estimated fair value of the Settlement Warrants was determined using the Black-Scholes pricing model. The estimated fair value of the Settlement Warrants was subject to revaluation at each balance sheet date and any changes in fair value were recorded as a non-cash gain or (loss) in the Statement of Operations as a component of operating expenses until the Settlement Warrants were issued. In addition, the fair value of the Settlement Warrants on June 30, 2018 was determined based on the estimated fair value of the Settlement Warrants at the time of issuance. We recorded non-cash gains of approximately $0.7 million in the nine

months ended September 30, 2018 in our Statement of Operations attributable to the decrease in the fair value of the Settlement Warrants prior to their issuance that principally resulted from a lower volatility rate relative to prior periods. In July 2018, upon the issuance of the Settlement Warrants, we reclassified the approximate $1.4 million value of the Settlement Warrants from a liability to stockholders equity as a component of additional paid-in capital based upon the terms of the warrant agreement and, accordingly, the approximate $1.4 million contingent liability on our balance sheet as of June 30, 2018 associated with the warrant portion of the settlement was eliminated.

Refer to Note 9, “Legal Proceedings” to our condensed consolidated financial statements and Part II, Item 1 under the heading “Legal Proceedings” included elsewhere in this Quarterly Report on Form 10-Q, for a further discussion of the Class Action settlement.

The key assumptions used to estimate the fair value of the Settlement Warrants were as follows:

	December 31, 2017	March 31, 2018	June 30, 2018
Expected price volatility	101.52%	96.01%	62.74%
Expected term (in years)	1.00	1.00	1.00
Risk-free interest rates	1.76%	2.09%	2.37%
Stock price	$ 2.79	$ 2.90	$ 2.90
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, 2018, we are forecasting a net loss for the year ended December 31, 2018 and an effective tax-rate of 0%, 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. On December 22, 2017, President Trump signed into law legislation commonly known as the Tax Cuts and Jobs Act, or the Act. The Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

On December 22, 2017, the U.S. Securities and Exchange Commission, or SEC, issued guidance under Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act directing taxpayers to consider the impact of the U.S. legislation as “provisional” when it does not have the necessary information available,

prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law. Our accounting treatment is expected to be completed in the fourth quarter of 2018 which is within the one-year period from the enactment date of the Act.

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 asset and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, 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, measurement of the PIPE Warrant liability, estimated settlement liabilities and stock-based compensation. 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 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, 2018, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2017, which we filed with the SEC on March 13, 2018, except as set forth below:

On January 1, 2018, we adopted ASC 606 using the modified retrospective method and applied the new guidance to the most current period presented with the cumulative effect of changes reflected in the opening balance of the accumulated deficit. The adoption of ASC 606 resulted in an approximate $2.7 million increase in each of deferred revenue and the accumulated deficit at the transition date. The transition adjustment related solely to our EUSA Agreement. The transition adjustment resulted from a change to our accounting policy with respect to the recognition of milestone payments as a result of adopting ASC 606. Refer to Note 3 – “Significant Accounting Policies - Revenue Recognition” and Note 4 – “Collaborations and License Agreements – EUSA”, to our condensed consolidated financial statements included elsewhere in this Quarterly Form 10-Q for further information.

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 Form 10-Q.

Results of Operations

Comparison of Three and Nine Months Ended September 30, 2018 and 2017

Revenues (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
EUSA	$467	$4,099	$(3,632)	(89)%	$1,926	$4,297	$(2,371)	(55)%
Novartis	—	15	(15)	(100)%	—	1,835	(1,835)	(100)%
CANbridge	2,000	500	1,500	300 %	2,000	1,000	1,000	100 %
Ophthotech	—	—	—	-%	—	115	(115)	(100)%
Other	—	—	—	-%	—	250	(250)	(100)%
Total	$2,467	$4,614	$(2,147)	(47)%	$3,926	$7,497	$(3,571)	(48)%

In 2018 as compared to 2017, revenue decreased under our partnership with EUSA by $3.6 million and $2.4 million in the three-month and nine-month periods, respectively, related to the European market approval of tivozanib. In August 2017, the European Commission approved tivozanib in first-line RCC in all 28 countries of the European Union, Norway and Iceland. Tivozanib, which triggered a $4.0 million research and development payment to us by EUSA, and is sold under the brand name FOTIVDA. In November 2017, we 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 commercially launched FOTIVDA in Germany, the United Kingdom and Austria. We earned sales royalties of $132,000 and $275,000 in the three months and nine months ended September 30, 2018, respectively.

Previously, under ASC 605, we recognized regulatory milestones when they were achieved. The $4.0 million research and development reimbursement payment upon marketing approval by the European Commission in RCC in August 2017 was recognized as revenue in the third quarter of 2017 in accordance with ASC 605-28, Revenue Recognition—Milestone Method. The impact of the adoption of ASC 606 on January 1, 2018 resulted in increases of approximately $2.7 million in each of deferred revenue and the accumulated deficit. This amount represents the $4.0 million gross amount of the research and development reimbursement payment for marketing approval by the European Commission in RCC, less the approximate $1.3 million that otherwise would have been recognized as collaboration and licensing revenue related to the cumulative catch-up for the period from contract execution in December 2015 through December 31, 2017, just prior to the adoption of ASC 606.

In February 2018, EUSA obtained reimbursement approval for tivozanib (FOTIVDA) from the NICE in the United Kingdom in first-line RCC and, accordingly, we earned a $2.0 million milestone payment from EUSA. In accordance with ASC 606, we recognized approximately $0.7 million of this milestone payment in 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 revenue over the remainder of our performance period through April 2022.

Refer to Note 4 “Collaborations and License Agreements – EUSA”, to our condensed consolidated financial statements included elsewhere in this Quarterly Form 10-Q, regarding the specific application of ASC 606 to our EUSA Agreement. Refer to Note 3 “Significant Accounting Policies – Recently Adopted Accounting Pronouncements”, to our condensed consolidated financial statements included elsewhere in this Quarterly Form 10-Q, for a comparison of revenue recognized during the three months and nine months ended September 30, 2018 under ASC 606 compared to the revenue that would have been recognized in that period had we continued to apply the provisions of ASC 605.

In 2018 as compared to 2017, revenue increased by $1.5 million and $1.0 million in the three-month and nine-month periods, respectively, under our partnership with CANbridge. In August 2018, CANbridge obtained regulatory approval from the CNDA of an IND application for a clinical study of AV-203 in ESCC and, accordingly, we earned a $2.0 million development and regulatory milestone payment. Also, CANbridge agreed to reimburse us $1.0 million for certain manufacturing costs and expenses incurred by us prior to the effective date of the CANbridge agreement with respect to AV-203. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, including one in March 2017 and one in September 2017. The timing and amount of revenue recognition for the payments received from CANbridge are the same under ASC 605 and ASC 606.

In 2018 as compared to 2017, revenue decreased by $1.8 million in the nine-month period under our former partnership with Novartis. In February 2017, Novartis paid $1.8 million out of its future payment obligations to us under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent’s on March 2, 2017.

Research and Development Expenses (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
Tivozanib	$3,962	$4,351	$(389)	(9)%	$13,324	$16,465	$(3,141)	(19)%
AV-380 Program in Cachexia	15	15	—	-%	72	1,835	(1,763)	(96)%
AV-203	667	—	667	100%	670	—	670	100%
Ficlatuzumab	133	43	90	209%	369	530	(161)	(30)%
Overhead	383	257	126	49 %	1,016	673	343	51 %
Total research and development expenses	$5,160	$4,666	$494	11 %	$15,451	$19,503	$(4,052)	(21)%

In 2018 as compared to 2017, research and development expenses increased in the three-month period by $0.5 million, principally due to a $0.7 million sublicense fee due to Biogen in connection with the $2.0 million development and regulatory milestone we earned under the CANbridge Agreement for regulatory approval from the CNDA of an IND application for a clinical study of AV-203 in ESCC. This increase was offset by a $0.4 million net decrease in tivozanib expenses that resulted from $1.2 million in decreases related to the year-to-year conduct of the

TIVO-3 and TiNivo trials that completed enrollment in 2017, offset by a $0.9 million increase for expenses related to the preparation of an NDA submission in anticipation of the results of the TIVO-3 topline data analysis. We initiated the TIVO-3 trial in May 2016 and completed enrollment in August 2017. In 2018 as compared to 2017, the majority of the patients are off treatment in the TIVO-3 trial compared to the trial being in active enrollment in the same period in 2017. We initiated the TiNivo trial in March 2017 and completed enrollment in December 2017.

In 2018 as compared to 2017, research and development expenses decreased in the nine-month period by $4.1 million, principally due to decreases of $3.1 million in net tivozanib expenses and $1.8 million in AV-380 for a time-based milestone obligation due to St. Vincent’s in the first quarter of 2017 that was not incurred in the same period in 2018, partially offset by the $0.7 million sublicense fee due to Biogen in connection with the $2.0 million development and regulatory milestone we earned under the CANbridge Agreement for regulatory approval from the CNDA of an IND application for a clinical study of AV-203 in ESCC.

The $3.1 million net decrease in tivozanib expenses principally included a $5.7 million net decrease in expenses related to the year-to-year conduct of the TIVO-3 and TiNivo trials that completed enrollment in 2017, partially offset by increases of $1.3 million for expenses related to the preparation of an NDA submission and $1.0 million for pre-commercial drug manufacturing, each in anticipation of the TIVO-3 topline data analysis, as well as a $0.6 million sublicense fee due to KHK in connection with the $2.0 million milestone we earned under our EUSA Agreement in February 2018 for reimbursement approval from the NICE in the United Kingdom in first-line RCC.

We anticipate that research and development expenses will continue to decrease during the remainder of 2018 as we seek to complete the TIVO-3 and TiNivo trials. This estimate excludes possible additional Company-sponsored clinical trials and any related drug manufacturing and drug supply distribution, and pre-commercialization activities that we may undertake following the positive topline results from the primary analysis of the TIVO-3 trial that we announced on November 5, 2018, subject to the availability of sufficient financial resources.

General and Administrative Expenses (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
General and administrative expenses	$2,719	$2,101	$618	29%	8,156	6,734	$1,422	21%

In 2018 as compared to 2017, general and administrative expenses increased in the three-month period by $0.6 million, principally due to increases of $0.2 million in professional fees, $0.1 million in compensation and benefits, and $0.3 million in non-cash stock-based compensation expense resulting from a higher stock price in 2018 as compared to 2017 in connection with annual stock option grants.

In 2018 as compared to 2017, general and administrative expenses increased in the nine-month period by $1.4 million, principally due to increases of $0.3 million in professional fees, $0.3 million in compensation and benefits, and $0.7 million in non-cash stock-based compensation expense resulting from a higher stock price in 2018 as compared to 2017 in connection with annual stock option grants.

We anticipate that general and administrative expenses will remain at current levels during the remainder of 2018, excluding pre-commercialization activities that we may undertake following the positive topline results from the primary analysis of the TIVO-3 trial that we announced on November 5, 2018, subject to the availability of sufficient financial resources.

Settlement Costs (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
Settlement costs	$ —	$ —	$ —	-%	$(667)	$ —	$(667)	100%

In December 2017, we entered into a MOU related to our class action settlement that included the issuance of the 2.0 million Settlement Warrants to purchase shares of our common stock. The Settlement Warrants were revalued at each balance sheet date prior to issuance. On July 16, 2018 the Company issued and delivered the Settlement Warrants. In addition, the fair value of the Settlement Warrants on June 30, 2018 was determined based on the estimated fair value of the Settlement Warrants at the time of issuance.

In July 2018, upon the issuance of the Settlement Warrants, we reclassified the approximate $1.4 million value of the Settlement Warrants from a liability to stockholders equity as a component of additional paid-in capital based upon the terms of the warrant agreement and, accordingly, the approximate $1.4 million contingent liability on our balance sheet as of June 30, 2018 associated with the warrant portion of the settlement was eliminated.

In 2018, settlement costs decreased in the nine-month period attributable to the decreases in the fair value of the Settlement Warrants that principally resulted from a lower volatility rate of our common stock used in the Black-Scholes valuations relative to prior periods.

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

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
Change in fair value of warrant liability	(16,172)	$(23,538)	$7,366	(31)%	$(6,512)	$(47,947)	$41,435	(86)%

In 2018, we recorded approximate non-cash losses of $16.2 million and $6.5 million in the three-month and nine-month periods, respectively, in our Statement of Operations attributable to the increases in the fair value of the PIPE Warrant liability that principally resulted from a higher stock price of $3.31 on September 30, 2018 compared to the stock prices of $2.26 on June 30, 2018 and $2.79 on December 31, 2017.

In 2017, we recorded approximate non-cash losses of $23.5 million and $47.9 million in the three-month and nine-month periods, respectively, in our Statement of Operations attributable to the increases in the fair value of the PIPE Warrant liability that principally resulted from a higher stock price of $3.65 on September 30, 2017 compared to the stock prices of $2.22 on June 30, 2017 and $0.54 on December 31, 2016.

Interest Expense, net (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
Interest expense, net	$(579)	$(655)	$ 76	(12)%	$(1,621)	$(1,736)	$ 115	(7)%

In December 2017, we refinanced our debt facility, the terms of which included a reduction in the then interest rate from 11.9% to 9.45%, an extension in the interest-only period by 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, and an extension in the loan maturity from December 2019 to July 2021. In June 2018, the interest rate increased from 9.45% to 9.70% due to a corresponding increase in the prime interest rate, which is a component of the overall interest rate.

We anticipate that interest expense in 2018 will continue to decrease due to the lower interest rates as a result of our debt refinancing in December 2017.

Provision for Income Taxes (in thousands)

	Three Months Ended September 30,		Comparison		Nine Months Ended September 30,		Comparison	
	2018	2017	$	%	2018	2017	$	%
Provision for income taxes	$ —	$ (51)	$ 51	(100)%	$ —	(101)	$ 101	(100)%

In 2017, we incurred a $50,000 tax provision for foreign withholding taxes in each of the first quarter and third quarter related to the $0.5 million reimbursement payments from CANbridge that we received in each of March 2017 and September 2017 for manufacturing development activities conducted by us prior to the effective date of the collaboration and license agreement. No foreign withholding taxes were incurred in the three months and nine months ended September 30, 2018.

Liquidity and Capital Resources

We have financed our operations to date primarily through the sale of 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, 2018, we had cash, cash equivalents and marketable securities of approximately $20.4 million. See "—Operating Capital Requirements 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, and U.S. government agency securities. 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,	
	2018	2017
Net cash used in operating activities	$(18,409)	$(15,415)
Net cash provided by (used in) investing activities	18,579	(12,843)
Net cash provided by financing activities	5,289	29,516
Net increase in cash and cash equivalents	$5,459	$1,258

Our operating activities used cash of $18.4 million and $15.4 million in 2018 and 2017, respectively. Cash used in operations was principally due to our net loss adjusted for non-cash items and changes in working capital.

Our investing activities provided cash of $18.6 million in 2018 and used cash of $12.8 million in 2017, principally due to net changes in the maturities and purchases of marketable securities.

Our financing activities provided cash of $5.3 million and $29.5 million in 2018 and 2017, respectively. In 2018, we raised approximately $5.8 million from the issuance of our common stock, including approximately $0.5 million from the exercise of 0.5 million PIPE Warrants in January 2018, approximately $5.1 million in net proceeds from an underwritten public offering of 2.5 million shares of our common stock in August 2018, and approximately $0.2 million from the exercise of stock options, offset by a $0.5 million end-of-term debt payment in January 2018 in connection with the 2014 Amendment of our loan First Loan Agreement with Hercules (all capitalized terms being defined in the section below, “Credit Facilities”). In 2017, we raised approximately $29.5 million in net proceeds, including $15.4 million from an underwritten public offering of 34.5 million shares of our common stock in March 2017, $8.8 million from sales of 6.5 million shares of our common stock under our FBR Sales Agreement and $5.0 million from additional borrowings under our loan agreement with Hercules in June 2017, and $0.3 million from the exercise of 0.3 million PIPE Warrants in July 2017.

Settlement Warrants

On July 16, 2018, we issued and delivered 2.0 million Settlement Warrants to purchase shares of our common stock for a one-year period after the date of issuance at an exercise price equal to $3.00 per share. Refer to the section above, “Class Action Settlement and Settlement Warrants” for further discussion.

Sales Agreement with Leerink

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. The 2017 Shelf was filed to replace our then-existing 2015 shelf registration statement, which was terminated upon the 2017 Shelf being declared effective by the SEC on December 15, 2017.

In February 2018, we entered into the Leerink Sales Agreement 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 Leerink as our sales agent, with any sales of common stock through 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. We agreed to pay Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. No shares of our common stock were sold under the Leerink Sales Agreement as of September 30, 2018.

In the fourth quarter of 2018 to-date, we sold approximately 3.8 million shares pursuant to the Leerink Sales Agreement, resulting in net proceeds of approximately $8.4 million, net of commissions.

Public Offering – August 2018

On August 21, 2018, we closed an underwritten public offering of 2.5 million shares of our common stock at the public offering price of $2.26 per share for gross proceeds of approximately $5.7 million. Two greater than 5% stockholders, including an entity affiliated with New Enterprise Associates and another stockholder purchased approximately 2.0 million shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to us were approximately $5.1 million after deducting underwriting discounts and estimated offering expenses payable by us.

Public Offering – March 2017

On March 31, 2017, we closed an underwritten public offering of 34.5 million shares of our common stock, including the exercise in full by the underwriter of its option to purchase 4.5 million shares, at the public offering price of $0.50 per share for gross proceeds of approximately $17.3 million. Certain of our executive officers and a director purchased an aggregate of 420,000 shares and an entity affiliated with New Enterprise Associates purchased 6.0 million shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting underwriting discounts and estimated offering expenses payable by us.

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 17,642,482 units, at a price of $0.965 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 $1.00 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 544,039 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, 2018, PIPE Warrants exercisable for 777,201 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 16,865,281 shares of common stock were outstanding. In July 2017, we issued to Hercules Capital Inc. 259,067 shares of common stock upon its exercise of all of its PIPE Warrants, and we received approximately $0.3 million in cash proceeds. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and we issued 518,134 shares of our common stock and received approximately $0.5 million in cash proceeds.

Credit Facilities

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, or the 2012 Amendment; September 2014, or the 2014 Amendment and May 2016, or the 2016 Amendment. 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, with Hercules Funding III, LLC and Hercules Capital, Inc., which we collectively refer to as Hercules.

Pursuant to the 2014 Amendment, we received $10.0 million in additional loan proceeds from Hercules and were required to make an end-of-term payment of approximately $0.5 million on January 1, 2018. This payment was made on the first business day of 2018.

Pursuant to the 2016 Amendment, we received additional loan proceeds from Hercules, in an aggregate amount of $10.0 million, received in installments of $5.0 million in each of May 2016 and June 2017, which increased the aggregate outstanding principal balance under the First Loan Agreement to $20.0 million. We are required to make an end-of-term payment totaling $0.3 million on December 1, 2019. The 2016 Amendment included a financial covenant that required us 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 were satisfactory to Hercules. Principal payments were scheduled to commence on January 1, 2018 and the loan was scheduled to mature on December 1, 2019.

In December 2017, we entered into 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 new $20.0 million loan facility has 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, Hercules did not receive any additional warrants to purchase shares of our common stock and no longer has the option, subject to our written consent, to participate in our future equity financings up to $2.0 million through the purchase of our common stock either with cash or through the conversion of outstanding principal under the loan.

Pursuant to the 2017 Loan Agreement, the loan maturity date has been revised from December 2019 to July 2021. We are not required to make principal payments until February 1, 2019, at which time we will be 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, which increases the total end-of-term payments under the 2014 Amendment, 2016 Amendment and 2017 Loan Agreement to approximately $1.6 million. The end-of-term payments under the 2014 Amendment, in the approximate amount of $0.5 million, and the 2016 Amendment, in the amount of $0.3 million, continue to be due on their original due dates of January 1, 2018 and December 1, 2019, respectively. 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 has been removed. Per the 2017 Loan Agreement, the interest rate decreased from 11.9% to 9.45%. The interest rate increased from 9.45% to 9.70% and from 9.70% to 9.95% in June 2018 and September 2018, respectively, due to the corresponding increases in the prime interest rates.

The interest-only period could be extended by two 6-month deferrals upon the achievement of specified milestones relating to the development of tivozanib, including (i) on or prior to September 30, 2018, we have received positive data with respect to our TIVO-3 trial for the treatment of RCC for patients in the third-line setting which positive data supports the filing for a new drug application with the Food and Drug Administration, or FDA, subject to confirmation by Hercules at its reasonable discretion, and (ii)

on or prior to June 28, 2019, we have received approval from the FDA for our tivozanib product for the treatment of RCC for patients in the third-line setting, subject to confirmation by Hercules at its reasonable discretion.

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%. Our annual interest rate as of September 30, 2018 was 9.95%.

We have determined that the risk of subjective acceleration under the material adverse events clause included in the 2017 Loan Agreement 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, 2018, 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 2017 Loan Agreement. The loans are secured by a lien on all of our personal property (other than intellectual property), whether owned as of, or acquired after, the date of the First Loan Agreement.

Operating Capital Requirements 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. We anticipate that we will continue to incur significant operating losses for the next several years as we incur expenses to continue to execute on our clinical development strategy to advance our preclinical and clinical stage assets. 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 our development activities for tivozanib. For example, we estimate that the aggregate remaining costs for the TIVO-3 trial, including drug supply and distribution, could be in the range of $4.0 million to $7.0 million through 2019. We estimate that the overall cost for the TIVO-3 trial, including drug supply and distribution, could be in the range of $45.0 million to $48.0 million. Our aggregate remaining costs for the TiNivo trial, including tivozanib drug supply and distribution, could be in the range of $0.8 million to $1.0 million through 2019. We estimate that the overall cost for the TiNivo trial, including drug supply and distribution, could be in the range of $4.0 million to $4.5 million. BMS is providing nivolumab for the TiNivo trial. In addition, in September 2017, EUSA elected to opt-in to co-develop the TiNivo trial and paid the maximum $2.0 million for its approximate 50% share of the total trial costs.

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

During the nine months ended September 30, 2018, we received approximately $10.0 million in funding, including the $2.0 million milestone payment by EUSA for the February 2018 reimbursement approval by the NICE for RCC in the United Kingdom, the $2.0 million milestone payment by CANbridge for the August 2018 regulatory approval from the CNDA of an IND application for a clinical study of AV-203 in ESCC, the approximate $5.1 million in net proceeds from the sale of 2.5 million shares of our common stock in a public offering in August 2018, approximately $0.2 million in royalties from the sales of FOTIVDA by EUSA, and approximately $0.7 million related to the exercise of PIPE Warrants and stock options.

As of September 30, 2018, we had approximately $20.4 million in cash, cash equivalents and marketable securities, working capital of $2.0 million and an accumulated deficit of $616.8 million. In the fourth quarter of 2018 to-date, we sold approximately 3.8 million shares of our common stock pursuant to our Leerink Sales Agreement and received approximately $8.4 million in net proceeds. Based on these available cash resources, we believe that we do not have sufficient cash on hand to support current operations for at least the next 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. In August 2017, EUSA obtained marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC.
- 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 possible additional sales of our common stock, including public or private equity financings.
- Partner our AV-353 platform to secure potential additional non-dilutive funds and advance development of the AV-353 platform for the potential treatment of PAH.

Pursuant to our EUSA Agreement, we are entitled to receive up to an additional $8.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy and Spain, 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, as mutually agreed by the parties. These milestone payments are subject to the 30% sublicense fee payable to KHK. We are also eligible to receive an additional research and development reimbursement payment from EUSA of 50% of the total costs for our TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that study. This research and development reimbursement payment would not be subject to the 30% sublicense fee payable to KHK, subject to certain limitations.

There can be no assurance, however, 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 at least the next twelve months from the date of filing this Quarterly Report on Form 10-Q.

Pursuant to the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern, management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management’s plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about our 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 our collaborators and other resources 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. Accordingly, substantial doubt is deemed to exist about our ability to continue as a going concern within one year after the date these financial statements are issued.

We believe that our approximate $20.4 million in cash, cash equivalents and marketable securities at September 30, 2018, along with approximately $8.4 million received in net proceeds from the sale of approximately 3.8 million shares of our common stock pursuant to the Leerink Sales Agreement in the fourth quarter of 2018 to-date, would allow us to fund our planned operations into the second quarter of 2019. This estimate assumes no receipt of additional milestone payments and royalties from our partners, no funding from new partnership agreements, no additional equity financings, no debt financings, no additional sales of equity under our Leerink Sales Agreement and no additional sales of equity through the exercise of our outstanding PIPE Warrants or the Settlement Warrants.

Accordingly, the timing and nature of activities contemplated for the remainder of 2018, 2019 and thereafter will be conducted subject to the availability of sufficient financial resources.

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 with Hercules or under any other agreements with third parties;
- the outcome of any legal actions against us;
- 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; 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 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, 2017 filed with the SEC on March 13, 2018.

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 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of September 30, 2018, we had cash, cash equivalents and marketable securities of approximately $20.4 million. Currently, our funds are invested in a U.S. government money market fund and corporate debt securities, including commercial paper, and U.S. government agency securities. We do not hold any of these instruments for trading or speculative purposes. Our funds are invested in accordance with investment guidelines as approved by our Board of Directors.

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term cash equivalents. Our cash equivalents and marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability to hold our cash equivalents until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments. We do not currently have any auction rate securities.

Our loans payable are subject to interest rate risk. As of September 30, 2018, our aggregate principal balance outstanding on our 2017 Loan Agreement with Hercules was $20.0 million. Per annum interest is payable on the principal balance of the loan each month it remains outstanding at the greater of 9.45% or 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%. As of September 30, 2018, the interest rate was 9.95%. For every 1% increase in the prime rate over 4.75%, given the amount of debt outstanding under the 2017 Loan Agreement as of September 30, 2018, we would have an increase in future annual cash outflows of approximately $0.2 million over the next twelve-month period as a result of such 1% increase.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations and investigational sites that are located around the world. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

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, 2018. 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 our Chief Financial Officer concluded that as of September 30, 2018, 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, 2018 that have materially affected, or is reasonably likely to materially affect, our internal control over financial reporting, except as noted below.

During the quarter ended March 31, 2018, we implemented internal controls to ensure we adequately evaluated our contracts and properly assessed the impact of ASC 606, to facilitate our adoption on January 1, 2018. In addition, we implemented certain additional controls in connection with the ongoing accounting for our revenue arrangements under ASC 606, including controls to re-evaluate the constraint on variable consideration at each reporting period.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

In June 2018, we settled a consolidated class action lawsuit, or the Class Action, In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, that had been filed in 2013 against us and certain of our former officers (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer, and Ronald DePinho) in the United States District Court for the District of Massachusetts, or the District Court. The 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. We moved to dismiss again, and the District Court ruled in our 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, or the Class, alleging claims similar to those alleged in the prior complaints, namely that we and certain of our 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 our 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, or MOU, to settle the Class Action. Under the terms of the MOU, we agreed to cause certain of our and the individual defendants' insurance carriers to provide the 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, we agreed to issue to the Class warrants, or the Settlement Warrants, for the purchase of 2.0 million shares of our common stock, which are exercisable, subject to certain conditions, 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, or 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 an order of final approval and final judgment. Upon the conclusion of a 30-day appeal period, and the occurrence of certain specified circumstances, the settlement become effective on June 29, 2018. On July 16, 2018, we 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.

In 2013, the SEC also served a subpoena on us for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC invited us to discuss the settlement of potential claims asserting that we violated federal securities laws by omitting to disclose to investors the recommendation by the staff of the FDA on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. On March 29, 2016, the SEC filed a complaint against us and three of our former officers in the District Court alleging that we misled investors about our efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the SEC's complaint, we consented to the entry of a final judgment pursuant to which we paid the SEC a $4.0 million civil penalty to settle the SEC's claims against us. On March 31, 2016, the District Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined us from violating Section 17(a) of the Securities Act of 1933, as amended, or the Securities Act, Sections 10(b) and 13(a) of the Exchange Act and rules 10b-5, 12b-20, 13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered us to pay the agreed-to civil

penalty. On September 15, 2017 and October 31, 2017, respectively, two of our former officers consented to entry of final judgment to settle the SEC's claims against them. We are not a party to the litigation between the SEC and the remaining former officer, and we can make no assurance regarding the outcome of that action or the SEC's claims against that individual.

Refer to Note 9 – "Legal Proceedings", in our condensed consolidated financial statements for further discussion.

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.

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 of September 30, 2018, we had approximately $20.4 million in cash, cash equivalents and marketable securities. In the fourth quarter of 2018 to-date, we sold approximately 3.8 million shares of our common stock pursuant to our Leerink Sales Agreement and received approximately $8.4 million in net proceeds. Based on these available cash resources, we believe we do not have sufficient cash on hand to support current operations for at least the next 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 these financial statements are issued. Management’s plans in this regard are described in Note 1 of the consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q However, 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 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 incurred a net loss of $27.1 million for the nine months ended September 30, 2018 and as of September 30, 2018, had an accumulated deficit of $616.8 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 our product candidates. As noted above, we and our auditors 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 beyond our cash runway. For example, we estimate that the aggregate remaining costs for the TIVO-3 trial, including drug supply and distribution, could be in the range of $4.0 million to $7.0 million through 2019. We estimate that the overall cost for the TIVO-3 trial, including drug supply and distribution, could be in the range of $45.0 million to $48.0 million. Our aggregate remaining costs for the TiNivo trial in collaboration with BMS and EUSA, including tivozanib drug supply and distribution, could be in the range of $0.8 million to $1.0 million through 2019. We estimate that the overall cost for the TiNivo trial, including drug supply and distribution, could be in the range of $4.0 million to $4.5 million. BMS is providing nivolumab for the TiNivo trial. In addition, in September 2017, EUSA elected to opt-in to co-develop the TiNivo trial and paid the maximum $2.0 million for its approximate 50% share of the total trial costs.

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

We believe that our approximately $20.4 million in cash, cash equivalents and marketable securities at September 30, 2018, along with approximately $8.4 million received in net proceeds from the sale of approximately 3.8 million shares of our common stock pursuant to the Leerink Sales Agreement in the fourth quarter of 2018 to-date, would allow us to fund our planned operations into the second quarter of 2019. This estimate assumes no receipt of additional milestone payments and royalties from our partners, no funding from new partnership agreements, no additional equity financings, no debt financings, no additional sales of equity under the Leerink Sales Agreement and no additional sales of equity through the exercise of our outstanding PIPE Warrants or Settlement Warrants. Accordingly, the timing and nature of activities contemplated for the remainder of 2018, 2019 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 loan agreement with Hercules, which we refer to as the 2017 Loan Agreement with Hercules, or under any other agreements with third parties;
- the outcome of any legal actions against us;
- 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; 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, Hercules may accelerate payments if we were to default under the Hercules Loan Agreement and 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.

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 marketing approval for tivozanib (FOTIVDA) received by our partner EUSA in August 2017, 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. Although we announced positive topline results from the primary analysis of the TIVO-3 trial in November 2018 and plan to submit an NDA to the FDA within approximately six months from our announcement, we may not be able to submit our NDA within that timeframe or at all. Any NDA we submit to the FDA may not be accepted for submission or approved by the FDA and even if approved, we may not be able to successfully commercialize tivozanib.

Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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 our Litigation

We have concluded a settlement with the SEC, but the SEC is still pursuing an action against our former officer.

We paid $4.0 million to settle a lawsuit filed by the SEC in federal court alleging that we violated federal securities laws by omitting to disclose the recommendation of the staff of the FDA, on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. See Part II, Item 1 of this Quarterly Report on Form 10-Q under the heading “Legal Proceedings” for a further discussion of these claims. The SEC also named three of our former officers as defendants in the same lawsuit. The SEC and two of our former officers have settled. The lawsuit against the remaining officer is still pending. We are not a party to the continuing litigation between the SEC and the former officer. However, that individual has and may continue to seek advancement of legal expenses or indemnification for any losses, either of which could be material to the extent not covered by our director and officer liability insurance.

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 European marketing approval for tivozanib received by our partner EUSA in August 2017, 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 our clinical trials of tivozanib, including the TIVO-3 trial and the TiNivo trial;

- 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;
- 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 KHK;
- protection of our rights in our intellectual property portfolio, including our ability to maintain our license agreement with KHK;
- 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 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 be more effective than other commercially available alternatives.

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 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 or undesirable side effects caused by, or other unexpected properties of, tivozanib or our other product candidates may be identified during development and 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 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 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;
- we may decide, or regulators or institutional review boards may require that we 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.

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;
- competing clinical trials; and
- 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.

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.

Results of early clinical trials may not be predictive of results of later clinical trials.

The outcome of early clinical trials, such as our phase 1b/2 TiNivo trial, may not be predictive of the success of later clinical trials. In addition, interim results and analyses of clinical trials, such as the immature OS data analyzed at the time of the final PFS analysis for our TIVO-3 trial, do not necessarily predict the final results or the success of a trial once it is complete. 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.

The design of a clinical trial can determine whether its results will support approval of a product, and 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 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 concern about the negative OS trend expressed in the complete response letter from June 2013. However, the TIVO-3 trial could fail to achieve its endpoints, or could otherwise be rejected by the FDA as a basis for marketing approval for another reason.

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.

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 a complete response letter 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 concern about the negative OS trend expressed in the complete response letter from June 2013. Although the TIVO-3 trial met its primary endpoint for PFS, the analysis of the secondary endpoint of OS was not mature at the time of the final PFS analysis, with only 46% of potential OS events having been reported. OS showed a hazard ratio of 1.06 with a p-value of 0.69 at the time of the preliminary OS analysis. If the TIVO-3 trial does not achieve a final OS result that is satisfactory to the FDA, or the FDA does not find the results of the TIVO-3 trial to adequately demonstrate a favorable risk-benefit profile for tivozanib in RCC, then the TIVO-3 trial could be rejected by the FDA as a basis for marketing approval.

If the FDA or other comparable foreign regulatory agency does not accept or approve 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.

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.

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 competitive therapies on the market 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. 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;

70

- 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 both their potential for marketing approval and commercialization. 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. 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 objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect any product candidate that we commercialize with our strategic partners will compete with existing, market-leading products.

There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our products, or with different types of products in the same indications we are pursuing. A number of multinational pharmaceutical companies, as well as large biotechnology companies, including, but not limited to, Amgen, Inc., Arqule, Inc., AstraZeneca, Bayer HealthCare AG, Bristol-Myers Squibb, Eisai Co., Ltd., Eli Lilly and Company, Exelixis, Inc., Gilead Sciences, Inc., GlaxoSmithKline plc, Helsinn and XBiotech, Incyte Corporation, Janssen Pharmaceuticals, Inc. (a division of Johnson and Johnson), Jazz Pharmaceuticals plc, Merck, Merrimack Pharmaceuticals, Inc., Novartis, Pfizer Inc. and Roche Laboratories, Inc. are pursuing development in diseases we focus on or are currently developing or marketing pharmaceuticals that target VEGFR, HGF, ErbB3, GDF15, Notch 3 or other pathways on which we may focus. It is probable that the number of companies seeking to develop competing products and therapies will increase.

Many of our competitors, either alone or with their strategic partners, have greater financial, technical and human resources than we do and greater experience in product discovery and development, obtaining FDA and other regulatory approvals, and commercialization. Many are already marketing products to treat the same indications, and having the same biological targets, as the product candidates we are developing, including with respect to renal cell carcinoma. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we effectively:

- 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.

There are currently 11 FDA-approved drugs in oncology which, like tivozanib, target the VEGFR pathway as a part or all of their inhibitory mechanism. Eight of the FDA-approved VEGFR pathway inhibitors are oral small molecule receptor TKIs. Many of the approved VEGFR pathway inhibitors are in ongoing development in additional cancer indications including RCC. Additionally, we are aware of a number of companies that have ongoing programs to develop both small molecules and biologics that target the VEGFR pathway. The emergence of PD-1/PD-L1 inhibitor and other immune system-targeted therapies, both alone and in combination, present additional competition for tivozanib in RCC. We are aware of several phase 3 registration studies evaluating PD-1/PD-L1 inhibitors in combination with VEGFR TKIs in RCC, as well as combinations of PD-1 agents with other immune therapies for RCC. The FDA approved the combination of Opdivo and Yervoy for first-line RCC patients with intermediate or poor risk prognosis in April 2018. In addition, the IMmotion151 Ph3 combination study of bevacizumab and atezolizumab

vs sunitinib in first-line RCC reported positive results for one of the co-primary endpoints (PFS), the JAVELIN Renal 101 Ph3 combination study of axitinib and avelumab vs sunitinib in first-line RCC reported positive results for one of the co-primary endpoints (PFS in PD-L1+ patients), and the KEYNOTE-426 Ph3 combination study of axitinib and pembrolizumab vs sunitinib in first-line RCC reported positive results for both primary endpoints of PFS and OS. If these additional combinations are approved, they could present additional competition for tivozanib.

We believe the products that are considered competitive with ficlatuzumab include those agents 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. There are also other agents that target ErbB3 as a part or all of their inhibitory mechanism. Only a limited number of agents have been approved for the treatment or prevention of cachexia caused by any disease. A number of agents with different mechanisms of action, however, have completed or are currently being studied in phase 2 trials in cachexia or muscle wasting. Currently, there are

no ongoing clinical trials of Notch 3-specific inhibitors or any approved Notch 3-specific inhibitors in PAH patients; however, there are multiple treatments approved for PAH through various mechanisms.

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 Pharma, 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 contract research organizations 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.

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, commonly referred to as 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 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 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. 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 manufacturers or we are unable to purchase these raw materials 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, quantity or timeframe necessary to develop and commercialize 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.

Any delay in entering into new strategic partnership agreements related to our product candidates could have an adverse effect on our business, including delaying the development and commercialization of our product candidates. If we are not able to establish and maintain strategic partnerships:

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

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. 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, on June 29, 2018, Novartis notified us that it was terminating the license agreement for our AV-380 program, without cause, effective August 28, 2018. During the term of the license agreement, Novartis was responsible for the costs and development of the program worldwide. We are currently evaluating options to continue the program's development.

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, 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 patient 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 U.S. under the Hatch-Waxman Act, by Supplementary Protection 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. patent covering the tivozanib molecule and its therapeutic use is 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 term of this patent until 2027. However, the length of the extension could be less than we request, or no extension may be granted at all. In addition, SPCs have been filed in over 15 European countries for the corresponding patents covering the tivozanib molecule, which, if granted, could extend the term of the such patents in each of those European countries until 2027. 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 United States Patent and Trademark Office, 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 tivozanib, we are aware of a third-party United States patent that contains broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation, and we have received written notice from the patent owners indicating that they believe we may need a license from them in order to avoid infringing their patent rights. 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 an 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 used in our AV-380 program, and from KHK 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.

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 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 major 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 recent events 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 U.S. The new patent law introduces changes including a first-to-file system for determining which inventors may be entitled to receive patents, and a new post-grant review process that allows third parties to challenge newly issued patents. It remains to be seen how the biopharmaceutical industry will be affected by such changes in the patent system. 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 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. Although we announced positive topline results from the primary analysis of the TIVO-3 trial in November 2018 and plan to submit an NDA to the FDA based on this data, we may not be able to obtain marketing approval from the FDA to successfully commercialize tivozanib in the United States. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations 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 a complete response letter 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.

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 European Union 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 European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. 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 European Union 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 European Union 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, the 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 or if we experience unanticipated problems with our product candidates, 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.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or 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 European Union 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 European Union'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. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires 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 requires 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 administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. 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 $10,781 to $21,563 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 2024 unless additional Congressional action is taken. 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 new 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.

With the Administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the ACA. For example, with enactment of the legislation commonly known as the Tax Cuts and Jobs Act of 2017, 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, will become 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. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing 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. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

The costs of prescription pharmaceuticals in the United States has 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 and proposed 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. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. 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 may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates 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 ability to generate revenues and become profitable could be impaired.

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 European Union, 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.

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.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we could incur liability, our competition position could be harmed, and our product development and commercialization efforts could be delayed.

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 will be 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.

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. We have completed several reductions in force related to restructurings we have completed in the past, which could make it more difficult to retain or attract employees in the future. 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. 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. 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, some or all 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;
- results of regulatory reviews relating to our product candidates;
- 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 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, since our May 2, 2013 announcement regarding the vote of the Oncologic Drugs Advisory Committee of the

FDA, we and

certain of our former officers and directors have been involved in a number of legal proceedings, including those described in Part II, Item 1 of this report under the heading “Legal Proceedings”. These proceedings and other similar litigation, if instituted against us, 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 time frames that we publicly estimate, 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 the AV-353 platform. 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, 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 current schedule for the achievement of key milestones under any of our programs. If we fail to achieve one or more of the milestones 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;
- changes in our 2017 Loan Agreement with Hercules, including the existence of any event of default that may accelerate payments due thereunder;
-

- non-cash changes in fair value related to re-valuations of our PIPE Warrant liability as a result of fluctuations in our stock price; and
- compliance with regulatory requirements.

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.

As widely reported, global credit and financial markets have been experiencing extreme volatility, and in some cases, disruptions, over the past several years. Although certain of these trends have recently showed signs of reversing, there can be no assurance that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will not occur. 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, 2018, we had approximately $20.4 million of cash, cash equivalents and marketable securities consisting of cash on deposit with banks, a U. S. government money market fund, corporate debt securities, including commercial paper, and 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. 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 or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents owned by us.

There is a possibility that our stock price may decline because of volatility of the stock market and general economic conditions.

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 event 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. 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.

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

We have incurred significant net losses since our inception and cannot guarantee when, if ever, we will become profitable. To the extent that we continue to generate federal and state taxable losses, unused net operating loss and tax credit carryforwards will carry forward to offset future taxable income, subject to applicable limitations on the use of those losses. Losses incurred in taxable years ending on or before December 31, 2017, are eligible to be carried forward for up to 20 years, and to be deducted in full against income for the years to which they may be carried. Losses incurred in taxable years ending after December 31, 2017, are eligible to be carried forward indefinitely, but may offset no more than 80% of the taxable income for the years to which they are carried (computed without regard to the deduction for carryovers of net operating losses). Net operating loss carryovers from periods ending on or before December 31, 2017, and tax credit carryovers from all periods could expire unused and be unavailable to offset future income tax liabilities.

In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or 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 over a three-year period, the corporation’s ability to use its pre-change net operating loss and credit carryovers to reduce its tax liability for post-change periods may be limited. We may experience ownership changes 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 carryover. A detailed study could result in adjustment to our research and development credit carryovers. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryovers 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.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Code. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is

uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Item 6. Exhibits.

Exhibit Index

Exhibit		Incorporated by Reference				Filed
Number	Description of Exhibit	Form	File Number	Date of Filing	Exhibit Number	Herewith
4.1	Warrant Agreement, dated July 16, 2018 by and among AVEO Pharmaceuticals, Inc. and Computershare Inc. and Computershare Trust Company, N.A. acting jointly as Warrant Agent.	8-K	001-34655	07/16/2018	4.1	
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	XBRL Instance Document.					X
101.SCH	XBRL Taxonomy Extension Schema Document.					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Label Linkbase Document.					X

101.PRE	XBRL Taxonomy Presentation Linkbase Document.	X

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, 2018 By: /s/ Matthew Dallas
Matthew Dallas
Chief Financial Officer and Principal Financial and Accounting Officer