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 June 30, 2019

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: 001-38537

AVROBIO, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**81-0710585**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Kendall Square Building 300, Suite 201 Cambridge, MA	**02139**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 914-8420

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**AVRO**	**Nasdaq Global Select Market**

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

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

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

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

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

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

As of August 5, 2019, the registrant had 31,663,232 shares of common stock, $0.0001 par value per share, outstanding.

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Forward-looking Information

This Quarterly Report on Form 10-Q contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- the timing, progress and results of preclinical studies and clinical trials for our programs and product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the existence or absence of side effects or other properties relating to our product candidates which could delay or prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences following any potential marketing approval;
- the timing, scope or likelihood of regulatory filings and approvals;
- our ability to develop and advance product candidates into, and successfully complete, clinical studies;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, product candidates, technology and plato platform, including our transition to a proprietary four-plasmid-produced lentiviral vector, or LV2, and our use of busulfan as a conditioning regimen administered through therapeutic drug monitoring, or TDM;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- the scalability and commercial viability of our manufacturing methods and processes, including our use of cryopreservation and implementation of a closed, automated manufacturing system;
- the rate and degree of market acceptance and clinical utility of our product candidates, in particular, and gene therapy, in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and/or our licensors are able to establish and maintain for intellectual property rights covering our product candidates;
- our financial performance;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- developments and projections relating to our competitors and our industry;
- our expectations related to the use of our cash reserves;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to remediate the material weaknesses that we and our independent registered public accounting firm identified and avoid any findings of material weaknesses or significant deficiencies in the future;
- the impact of laws and regulations, including without limitation recently enacted tax reform legislation;
- our expectations regarding the time during which we are an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act; and
- other risks and uncertainties, including those listed under the caption "Risk Factors"

All of our forward-looking statements are as of the date of this Quarterly Report on Form 10-Q only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Quarterly Report on Form 10-Q or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission (the SEC) could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q that modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited)
(in thousands, except share and per share data)

	June 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 90,348	$ 126,302
Prepaid expenses and other current assets	7,840	3,718
Total current assets	98,188	130,020
Property and equipment, net	2,741	2,634
Other assets	1,060	825
Total assets	$ 101,989	$ 133,479
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,572	$ 2,784
Accrued expenses and other current liabilities	6,193	7,822
Total current liabilities	8,765	10,606
Deferred rent, net of current portion	590	689
Total liabilities	9,355	11,295
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of June 30, 2019 and December 31, 2018	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized as of June 30, 2019 and December 31, 2018; 24,187,052 and 23,959,903 shares issued as of June 30, 2019 and December 31, 2018, respectively; 24,095,287 and 23,806,628 shares outstanding as of June 30, 2019 and December 31, 2018, respectively	2	2
Additional paid-in capital	197,529	193,921
Accumulated deficit	(104,897)	(71,739)
Total stockholders' equity	92,634	122,184
Total liabilities and stockholders' equity	$ 101,989	$ 133,479

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(unaudited)
(in thousands, except share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development	$ 12,267	$ 7,407	$ 24,713	$ 13,054
General and administrative	4,345	2,140	9,599	4,281
Total operating expenses	16,612	9,547	34,312	17,335
Loss from operations	(16,612)	(9,547)	(34,312)	(17,335)
Other income (expense):				
Interest income	565	234	1,222	392
Change in fair value of preferred stock warrant liability	—	(150)	—	(162)
Change in fair value of derivative liability	—	(1,042)	—	(1,629)
Other expense	(8)	(2)	(68)	(15)
Total other income (expense), net	557	(960)	1,154	(1,414)
Net loss	$ (16,055)	$ (10,507)	$ (33,158)	$ (18,749)
Comprehensive loss	$ (16,055)	$ (10,507)	$ (33,158)	$ (18,749)
Reconciliation of net loss to net loss attributable to common stockholders:				
Net loss	$ (16,055)	$ (10,507)	$ (33,158)	$ (18,749)
Accretion of issuance costs on redeemable convertible preferred stock	—	—	—	(2,243)
Net loss attributable to common stockholders—basic and diluted	$ (16,055)	$ (10,507)	$ (33,158)	$ (20,992)
Net loss per share attributable to common stockholders—basic and diluted (Note 10)	$ (0.67)	$ (2.98)	$ (1.38)	$ (7.16)
Weighted-average number of common shares used in computing net loss per share attributable to common stockholders—basic and diluted	24,046,262	3,529,269	23,985,717	2,930,358

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CONDENSED CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(unaudited)
(in thousands, except share data)

	Series Seed Redeemable Convertible Preferred Stock		Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	(Deficit) Equity
Balance as of December 31, 2018	—	$ —	—	$ —	—	$ —	23,806,628	$ 2	$ 193,921	$ (71,739)	$ 122,184
Stock-based compensation expense	—	—	—	—	—	—	—	—	1,455	—	1,455
Exercise of stock options	—	—	—	—	—	—	116,859	—	252	—	252
Vesting of restricted stock awards	—	—	—	—	—	—	30,753	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	(17,103)	(17,103)
Balance as of March 31, 2019	—	$ —	—	$ —	—	$ —	23,954,240	$ 2	195,628	$ (88,842)	$ 106,788
Stock-based compensation expense	—	—	—	—	—	—	—	—	1,663	—	1,663
Exercise of stock options	—	—	—	—	—	—	110,290	—	238	—	238
Vesting of restricted stock awards	—	—	—	—	—	—	30,757	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	(16,055)	(16,055)
Balance as of June 30, 2019	—	$ —	—	$ —	—	$ —	24,095,287	$ 2	$ 197,529	$ (104,897)	$ 92,634

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CONDENSED CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) - CONTINUED
(unaudited)
(in thousands, except share data)

	Series Seed Redeemable Convertible Preferred Stock		Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance as of December 31, 2017	3,333,333	$ 1,500	31,450,499	$ 25,000	—	—	2,305,173	$ —	$ 339	$ (23,474)	$ (23,135)
Issuance of series B redeemable convertible preferred stock, net of issuance costs of $2,243	—	—	—	—	28,285,557	58,257	—	—	—	—	—
Issuance of series B redeemable convertible preferred stock to settled accrued liability of license cost	—	—	—	—	233,765	500	—	—	—	—	—
Accretion of issuance costs related to redeemable convertible preferred stock	—	—	—	—	—	2,243	—	—	(339)	(1,904)	(2,243)
Stock-based compensation expense	—	—	—	—	—	—	—	—	109	—	109
Vesting of restricted stock awards	—	—	—	—	—	—	30,753	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	(8,242)	(8,242)
Balance as of March 31, 2018	3,333,333	1,500	31,450,499	25,000	28,519,322	61,000	2,335,926	—	109	(33,620)	(33,511)
Issuance common stock (IPO), net of issuance costs of $10,487	—	—	—	—	—	—	6,035,151	1	104,181	—	104,182
Stock-based compensation expense	—	—	—	—	—	—	—	—	457	—	457
Vesting of restricted stock awards	—	—	—	—	—	—	30,759	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	(10,507)	(10,507)
Conversion of redeemable convertible preferred stock into common stock	(3,333,333)	(1,500)	(31,450,499)	(25,000)	(28,519,322)	(61,000)	15,320,213	1	87,499	—	87,500
Reclassification of warrants to purchase shares of redeemable convertible preferred stock into warrants to purchase common stock	—	—	—	—	—	—	—	—	197	—	197
Balance as of June 30, 2018	—	—	—	—	—	—	23,722,049	$ 2	$ 192,443	$ (44,127)	$ 148,318

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(unaudited)
(in thousands)

	Six Months Ended June 30,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (33,158)	$ (18,749)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	390	66
Stock-based compensation expense	3,118	566
Amortization of deferred offering costs	—	22
Impairment loss of property and equipment	—	235
Deferred rent expense	(81)	(23)
Change in fair value of preferred stock warrant liability	—	162
Change in fair value of derivative liability	—	1,629
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,121)	(768)
Other assets	(57)	(300)
Accounts payable	26	3,029
Accrued expenses and other current liabilities	(1,820)	(98)
Net cash used in operating activities	(35,703)	(14,229)
Cash flows from investing activities:		
Change in restricted cash	—	24
Purchases of property and equipment	(741)	(424)
Net cash used in investing activities	(741)	(400)
Cash flows from financing activities:		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	58,258
Proceeds from exercise of stock options	490	—
Proceeds from issuance of common shares upon completion of initial public offering costs, net of offering costs	—	105,423
Net cash provided by financing activities	490	163,681
Net (decrease) increase in cash, cash equivalents and restricted cash	(35,954)	149,052
Cash, cash equivalents and restricted cash at beginning of period	126,794	5,963
Cash, cash equivalents and restricted cash at end of period	$ 90,840	$ 155,015
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ 10	$ 756
Property and equipment held for sale	$ —	$ 19
Deferred offering costs included in accrued expenses	$ 180	$ 1,241
Purchase of property and equipment paid for by landlord	$ —	$ 842
Accretion of issuance costs related to redeemable convertible preferred stock	$ —	$ 2,240
Reconciliation of cash, cash equivalents and restricted cash reported within the condensed consolidated balance sheets:		
Cash and cash equivalents	$ 90,348	$ 154,991
Long-term restricted cash (included in other assets)	492	24
Cash, cash equivalents and restricted cash at end of period	$ 90,840	$ 155,015

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

1. Nature of the Business

AVROBIO, Inc. (the "Company" or "AVROBIO") is a clinical stage gene therapy company focused on developing potentially curative *ex vivo* lentiviral gene therapies to treat rare diseases following a single dose.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

On June 20, 2018, the Company's registration statement on Form S-1 relating to its initial public offering ("IPO") was declared effective by the SEC. The IPO closed on June 25, 2018 and the Company issued and sold 5,247,958 common shares at a public offering price of $19.00 per share for net proceeds of $90,103 after deducting underwriting discounts and commissions of $6,980 and other offering expenses of approximately $2,628. Simultaneously, on June 25, 2018, the Company issued and sold 787,193 additional common shares, pursuant to the full exercise of the underwriters' option to purchase additional shares, for net proceeds of $13,910 after deducting underwriting discounts and commissions of $1,047. Thus, the aggregate net proceeds to the Company from the IPO, after deducting underwriting discounts and commissions and other offering costs, were $104,013. Upon the closing of the IPO, all series Seed redeemable convertible preferred stock (the "Series Seed Preferred Stock"), series A redeemable convertible preferred stock (the "Series A Preferred Stock") and series B redeemable convertible preferred stock (the "Series B Preferred Stock"), (the Series Seed Preferred Stock, the Series A Preferred Stock and the Series B Preferred Stock are collectively referred to as the "Preferred Stock") then outstanding converted into an aggregate of 15,320,213 shares of common stock. In July 2019, the Company closed an underwritten public offering of 7,475,000 shares of its common stock at a public offering price of $18.50 per share, which included 975,000 shares of the Company's common stock resulting from the full exercise of the underwriters' option to purchase additional shares at the public offering price, less underwriting discounts and commissions. The net proceeds to the Company from this offering, after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company, were approximately $129,500.

Through June 30, 2019, the Company has funded its operations primarily with proceeds from the sale of the Preferred Stock and common stock through the Company's IPO. The Company has incurred recurring losses since its inception, including net losses of $33,158 and $18,749 for the six months ended June 30, 2019 and 2018, respectively. In addition, as of June 30, 2019, the Company had an accumulated deficit of $104,897. Although the Company has incurred recurring losses and expects to continue to incur losses for the foreseeable future, the Company expects that its existing cash, cash equivalents and marketable securities will be sufficient to fund current planned operations and capital expenditure requirements for at least the next twelve months from the date of issuance of the financial statements contained in this Form 10-Q. However, the future viability of the Company is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

The unaudited condensed consolidated interim financial statements have been prepared on the same basis as the audited annual consolidated financial statements as of and for the year ended December 31, 2018, and, in the opinion of management, reflect all adjustments, consisting of normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of June 30, 2019, and the results of its operations for the three and six months ended June 30, 2019 and 2018, its statements of stockholders' equity for the three and six months ended June 30, 2019 and 2018 and its statement of cash flows for the six months ended June 30, 2019 and 2018.

The results for the three and six months ended June 30, 2019 are not necessarily indicative of the results to be expected for the year ending December 31, 2019, any other interim periods, or any future year or period. These interim financial statements should be read in conjunction with the audited financial statements as of and for the year ended December 31, 2018, and the notes thereto, which are included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the Securities and Exchange Commission ("SEC") on March 25, 2019.

The accompanying Unaudited Condensed Consolidated Financial Statements reflect the application of certain significant accounting policies as described below and elsewhere in these notes to the Unaudited Condensed Consolidated Financial Statements. As of June 30, 2019, there have been no changes to the Company's significant accounting policies as described in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, stock-based compensation expense, the valuation of equity and derivative instruments and the recoverability of the Company's net deferred tax assets and related valuation allowance. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Emerging Growth Company Status

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. The Company may take advantage of these exemptions until the Company is no longer an "emerging growth company." Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of an offering or such earlier time that it is no longer an "emerging growth company".

Subsequent Event Considerations

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the consolidated financial statements to provide additional evidence for certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required. See Note 13.

Recently Issued Accounting Pronouncements

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808)—Clarifying the Interaction between Topic 808 and Topic 606* ("ASU 2018-18"). The amendments in ASU 2018-18 clarify that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account. The amendments under ASU 2018-18 are effective for interim and annual fiscal periods beginning after December 15, 2019, with early adoption permitted. The amendments in ASU 2018-18 should be applied retrospectively to the date of initial application of ASC 606. The Company does not expect the adoption of ASU 2018-18 to have a material impact on its consolidated financial statements.

(in thousands, except share and per share data)

In August 2018, the FASB issued ASU No. 2018-15, *Intangible-Goodwill and Other Internal-Use Software (Subtopic 350-40)* ("ASU 2018-15"). ASU 2018-15 updates guidance regarding accounting for implementation costs associated with a cloud computing arrangement that is a service contract. The amendments under ASU 2018-15 are effective for interim and annual fiscal periods beginning after December 15, 2019, with early adoption permitted. The Company does not expect the adoption of ASU 2018-15 to have a material impact on its consolidated financial statements.

In August 2018, The FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*, or ASU 2018-13. The amendments in ASU 2018-13 eliminate, add, and modify certain disclosure requirements for fair value measurements. The amendments are effective for interim and annual reporting periods beginning after December 15, 2019, with early adoption permitted for either the entire ASU or only the provisions that eliminate or modify requirements. The amendments with respect to changes in unrealized gains and losses, the range and weighted-average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty are to be applied prospectively. All other amendments are to be applied retrospectively to all periods presented. The Company is currently evaluating the effects the adoption of ASU 2018-13 will have on its disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. For public entities, the standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. For all other entities, the standard is effective for fiscal years beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. The Company adopted ASU 2016-15 during the quarter ended March 31, 2019. The adoption did not have a material impact on the condensed consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02*, Leases (Topic 842)* ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases today. ASU 2016-02 supersedes the previous leases standard, ASC 840, *Leases*. For public entities, not-for-profit entities and an employee benefit plan that files financial statements with the U.S. Securities and Exchange Commission (SEC), the standard is effective for public entities for annual periods beginning after December 15, 2018 including interim periods within those fiscal years. For all other entities, the standard is effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

3. Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values as of June 30, 2019 and December 31, 2018:

	Fair Value Measurements as of June 30, 2019 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 90,173	$ —	$ —	$ 90,173
Restricted cash	492	—	—	492
	$ 90,665	$ —	$ —	$ 90,665

(in thousands, except share and per share data)

	Fair Value Measurements as of December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 126,047	$ —	$ —	$ 126,047
Restricted cash	492	—	—	492
	$ 126,539	$ —	$ —	$ 126,539

There were no transfers within the hierarchy during the six months ended June 30, 2019 or the year ended December 31, 2018.

Valuation of the Warrant to Purchase Preferred Stock

At June 30, 2018, the Company had outstanding a warrant to purchase shares of common stock that was issued to a lender in connection with a loan and security agreement entered into in 2017. The warrant was originally issued as a warrant to purchase shares of Series A Preferred Stock prior to the IPO. The fair value of the warrant to purchase preferred stock was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

Prior to the IPO, the Company classified the warrant as a liability on its consolidated balance sheets as the warrant is a free-standing financial instrument that may require the Company to transfer assets upon exercise. The preferred stock warrant liability was initially recorded at fair value upon the date of issuance and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant to purchase preferred stock were recognized as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss.

The Company utilized the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the warrant. The Company assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement included the fair value per share of the underlying redeemable convertible preferred stock issuable upon exercise of the warrant, the remaining contractual term of the warrant, the risk-free interest rate, the expected dividend yield and the expected volatility of the price of the underlying redeemable convertible preferred stock. Upon the IPO, the warrant to purchase preferred stock was converted to a warrant to purchase common stock. The carrying amount of warrant to purchase preferred stock as of the date of IPO was transferred to additional paid in capital.

The Company recognized a loss of $150 and $162 in the condensed consolidated statements of operations and comprehensive loss for the three and six months ended June 30, 2018, respectively, related to the change in fair value of the warrant.

Valuation of Derivative

In January 2016, in connection with a license agreement entered into with University Health Network ("UHN"), and as part of the initial consideration for the license, the Company issued 1,161,665 shares of common stock to UHN pursuant to a stock purchase agreement (the "Stock Purchase Agreement"). The Stock Purchase Agreement contained a provision requiring the Company to make a cash payment to UHN of up to $2,000 if UHN's fully diluted ownership was reduced within specified percentages as part of an IPO by the Company. The Company concluded the anti-dilution feature represented a derivative instrument and should be measured at fair value, with changes in fair value recognized as a gain or loss to other income (expense), net in the consolidated statements of operations and comprehensive loss. The initial fair value of the derivative was recorded as research and development expense in January 2016.

On June 21, 2018, in connection with the Company's IPO, the Company remeasured the fair value of the derivative to $2,000 as the Company was required to pay the dilution payment as mentioned above, which the Company paid in July 2018. An increase in fair value of $1,042 and $1,629 was recorded in other expense in the accompanying condensed consolidated statements of operations and comprehensive loss for the three and six months ended June 30, 2018, respectively.

(in thousands, except share and per share data)

4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	June 30, 2019	December 31, 2018
Tax incentive refund	$ 1,549	$ 1,325
Prepaid research and development costs	4,090	981
Prepaid insurance	1,626	316
Interest income receivable	163	220
Prepaid rent	83	81
Other current assets	329	795
	$ 7,840	$ 3,718

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	June 30, 2019	December 31, 2018
Laboratory and office equipment	$ 2,120	$ 1,624
Leasehold improvements	1,260	1,260
Computer equipment and software	135	134
	3,515	3,018
Less: Accumulated depreciation and amortization	(774)	(384)
	$ 2,741	$ 2,634

Depreciation and amortization expense for the three months ended June 30, 2019 and 2018 was $200 and $45, respectively. Depreciation and amortization expense for the six months ended June 30, 2019 and 2018 was $390 and $66, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	June 30, 2019	December 31, 2018
Compensation and benefit costs	$ 2,118	$ 2,616
Research and development costs	3,253	3,969
Consulting and professional fees	401	320
Other liabilities	421	917
	$ 6,193	$ 7,822

7. Redeemable Convertible Preferred Stock and Common Stock

Redeemable Convertible Preferred Stock

Prior to the IPO, the authorized capital stock of the Company included 63,491,857 shares of $0.0001 par value preferred stock, of which 3,333,333 shares have been designated as Series Seed Preferred Stock, 31,639,202 shares have been designated as Series A Preferred Stock and 28,519,322 shares have been designated as Series B Preferred Stock.

In January 2018, the Company issued and sold 28,519,322 shares of Series B Preferred Stock, at a price of $2.1389 per share, for total proceeds of $58,757, net of issuance costs of $2,243.

(in thousands, except share and per share data)

Upon closing of the IPO, all outstanding shares of Preferred Stock were converted into 15,320,213 shares of common stock. The holders of the Company's Preferred Stock had certain voting, dividend, and redemption rights, as well as liquidation preferences and conversion privileges. All rights, preferences, and privileges associated with the preferred stock were terminated at the time of the Company's IPO in conjunction with the conversion of all outstanding shares of Preferred Stock into shares of common stock.

Common Stock

As of June 30, 2019 and December 31, 2018, the authorized capital stock of the Company included 150,000,000 shares of common stock, $0.0001 par value and 10,000,000 shares of undesignated preferred stock. As of June 30, 2019 and December 31, 2018, no undesignated preferred stock was outstanding.

In accordance with the Fourth Amended and Restated Certificate of Incorporation, the holders of the common stock shall have the exclusive right to vote for the election of directors of the Company and on all other matters requiring stockholder action, each outstanding share entitling the holder thereof to one vote on each matter properly submitted to the stockholders of the Company for their vote; provided, however, that, except as otherwise required by law, holders of common stock, as such, shall not be entitled to vote on any amendment to any amendment to a certificate of designations of any series of undesignated preferred stock that alters or changes the powers, preferences, rights or other terms of one or more outstanding series of undesignated preferred stock if the holders of such affected series of undesignated preferred stock are entitled to vote, either separately or together with the holders of one or more other such series, on such amendment pursuant to a certificate of designations of any series of undesignated preferred stock.

Through June 30, 2019, no cash dividends have been declared or paid.

Common Stock Reserved for Future Issuance

At June 30, 2019 and December 31, 2018, the Company has reserved the following shares of common stock for future issuance:

	June 30, 2019	December 31, 2018
Shares reserved for vesting of restricted stock awards	94,065	153,276
Shares reserved for exercise of outstanding stock options	2,957,457	2,164,101
Shares reserved for issuance under the 2018 Stock Option and Grant Plan	435,834	385,561
Shares reserved for issuance under the 2018 Employee Stock Purchase Plan	461,266	223,200
Total shares of authorized common stock reserved for future issuance	3,948,622	2,926,138

8. Stock-Based Compensation

Stock Option Valuation

The assumptions that the Company used to determine the grant-date fair value of stock options granted to employees and members of the Board were as follows, presented on a weighted-average basis:

	Six Months Ended June 30,	
	2019	2018
Expected option life (years)	6.03	6.06
Risk-free interest rate	2.54%	2.73%
Expected volatility	80.86%	83.86%
Expected dividend yield	—%	—%

(in thousands, except share and per share data)

The following table summarizes the Company's stock option activity for the six months ended June 30, 2019:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2018	2,164,100	$ 7.75	8.77	$ 23,083
Granted	1,094,879	$ 16.22		
Exercised	(227,149)	$ 2.16		
Cancelled or forfeited	(74,373)	$ 4.15		
Outstanding as of June 30, 2019	2,957,457	$ 11.41	8.80	$ 18,956
Exercisable as of June 30, 2019	669,887	$ 2.59	7.68	$ 9,224
Vested and expected to vest as of June 30, 2019	2,957,457	$ 11.41	8.80	$ 18,956

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the underlying stock options and the estimated fair value of the Company's common stock for those stock options that had exercise prices lower than the estimated fair value of the Company's common stock.

The weighted-average grant-date fair value of the Company's stock options granted during the six months ended June 30, 2019 and 2018 was $11.37 and $7.63, respectively.

Restricted Common Stock

The following table summarizes the Company's restricted common stock activity for the six months ended June 30, 2019:

	Number of Shares	Weighted-Average Grant Date Fair Value
Issued and unvested as of December 31, 2018	153,275	$ 0.42
Granted	2,300	$ 15.65
Vested	(61,510)	$ 0.42
Forfeited, canceled or expired	—	$ —
Issued and unvested as of June 30, 2019	94,065	$ 0.42

The total fair value of restricted common stock vested during the six months ended June 30, 2019 and 2018 was $29 and $26, respectively.

Stock-Based Compensation

Stock-based compensation expense was allocated as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 901	$ 151	$ 1,761	$ 187
General and administrative	762	306	1,357	379
Total stock-based compensation expense	$ 1,663	$ 457	$ 3,118	$ 566

As of June 30, 2019, total unrecognized compensation cost related to the unvested stock-based awards was $21,334, which is expected to be recognized over a weighted-average period of 3.39 years.

9. License Agreements

Agreements with UHN

Fabry License Agreement—

On January 27, 2016, the Company entered into an agreement with UHN, pursuant to which UHN granted the Company an option to enter into an exclusive license under the UHN intellectual property related to Fabry disease in accordance with the pre-negotiated licensing terms. On November 4, 2016, the Company exercised its option and entered into a license agreement with UHN, pursuant to which UHN granted the Company an exclusive worldwide license under certain intellectual property rights and a non-exclusive worldwide license under certain know-how, in each case subject to certain retained rights, to develop, commercialize and sell products for use in the treatment of Fabry disease. In addition, for three years following the execution of the agreement, UHN granted the Company an exclusive option to obtain a license under certain improvements to the licensed intellectual property rights as well as an option to negotiate a license under certain other improvements.

Under this agreement, the Company paid an option fee of CAD $20, an upfront license fee of CAD $75, plus the annual license maintenance fee for the first year. Thereafter, the Company is also required to pay UHN future annual license maintenance fees until the first sale of a licensed product in certain markets. The Company is also obligated to make future milestone payments in an aggregate amount of up to CAD $2,450 upon the achievement of specified milestones as well as royalties on a country-by-country basis of a low to mid-single-digit percentage of annual net sales of licensed products and a lower single-digit royalty percentage in certain circumstances. Additionally, the Company has agreed to pay a low double-digit royalty percentage of all sublicensing revenue.

The agreement requires the Company to meet certain performance milestones within specified timeframes. UHN may terminate the agreement if the Company fails to meet these performance milestones despite using commercially reasonable efforts and the Company is unable to reach agreement with UHN on revised timeframes. The Company's royalty obligation expires on a licensed product-by-licensed product and country-by-country basis upon the latest to occur of the expiration or termination of the last valid claim under the licensed intellectual property rights in such country, the tenth anniversary of the first commercial sale of such licensed product in such country and the expiration of any applicable regulatory exclusivity in such country.

Unless terminated earlier, the agreement expires upon the expiration of the Company's royalty obligation for all licensed products. UHN can terminate the agreement if the Company fails to make any payments within a specified period after receiving written notice of such failure, or in the event that the Company fails to obtain or maintain insurance. Either the Company or UHN may terminate the license agreement in the event of a material breach by the other party and failure to cure such breach within a certain period of time. The Company can voluntarily terminate the agreement with prior notice to UHN.

For the three months ended June 30, 2019 and 2018, the Company recorded research and development expense related to this agreement with UHN of $132 and zero, respectively, which consists of reimbursable funded study trial costs. For the six months ended June 30, 2019 and 2018, the Company recorded research and development expense related to this agreement with UHN of $325 and zero, respectively, which consists of reimbursable funded study trial costs. No milestone or maintenance fees were incurred related to the Fabry license agreement in the six months ended June 30, 2019 and 2018.

Interleukin 12 License Agreement—

On January 27, 2016, the Company entered into an exclusive license agreement with UHN, pursuant to which UHN granted the Company a license to certain patent rights for the commercial development, manufacture, distribution and use of any products or processes resulting from development of those patent rights related to Interleukin 12. Upon execution of this agreement, the Company paid an upfront license fee of CAD $264. In addition, as part of the initial consideration for the license, the Company issued to UHN 1,161,665 shares of the Company's common stock. The fair value of the shares issued to UHN of $480 and the upfront fee was expensed upon the execution of the agreement. In addition, the Company agreed to pay UHN up to $2,000 upon the closing of an IPO if certain criteria are met. This obligation was considered a derivative instrument and was initially recorded at fair value of $49 (Note 3). The Company is also required to pay UHN future annual license maintenance fees of CAD $50 on each anniversary of the effective date of the license agreement prior to expiration or termination and potential future milestone payments of up to CAD $19,275 upon the achievement of specified clinical and regulatory milestones. The Company also agreed to pay UHN royalties of a low single-digit percentage of net sales of licensed products sold by the Company. If the Company grants any sublicense rights under the license agreement, the Company has agreed to pay UHN a low double-digit royalty percentage of any sublicense income received by the Company.

The agreement requires the Company to meet certain diligence requirements based upon specified milestones. The agreement expires on the later of the date the last patent rights expire in the last country or ten years from the date of first sale. UHN can terminate the agreement if the Company fails to make any payments within a specified period after receiving written notice of such failure, or in the event that the Company fails to obtain or maintain insurance. The Company can voluntarily terminate the agreement with prior notice to UHN. Either the Company or UHN may terminate the license agreement in the event of a material breach by the other party and failure to cure such breach within a certain period of time.

For the three and six months ended June 30, 2019 and 2018, the Company recorded research and development expense related to this agreement with UHN of $38 and $41, respectively, which consists of license maintenance fees. No license maintenance fees were recorded in the three months ended June 30, 2019 and 2018. No milestone fees were incurred related to the IL-12 license agreement in the six months ended June 30, 2019 and 2018.

Agreement with BioMarin Pharmaceutical Inc. ("BioMarin")

On August 31, 2017, the Company entered into a license agreement with BioMarin, pursuant to which BioMarin granted the Company an exclusive worldwide license under certain intellectual property rights owned or controlled by BioMarin to develop, commercialize and sell products for use in the treatment of Pompe disease. As consideration for this agreement, the Company paid an upfront license fee of $500 in cash and issued 233,765 shares of Series B Preferred Stock to BioMarin at the time of our Series B Preferred Stock financing in January 2018. Both the upfront cash payment of $500 and the value of the shares Series B Preferred Stock issued of $500 were recorded as research and development expense during the year ended December 31, 2017. The Company is also obligated to make future milestone payments of up to $13,000 upon the achievement of certain specified milestones and agreed to pay BioMarin royalties of a low single-digit percentage of net sales of licensed products sold by the Company or its affiliates covered by patent rights in a relevant country. No milestone fees related to the license were recorded for the six months ended June 30, 2019 and 2018.

Unless terminated earlier, the agreement expires upon the expiration of the Company's royalty obligation for all licensed products throughout the world. BioMarin and the Company can terminate the agreement in the event of a material breach by the other party and failure to cure such breach within a certain period of time. The Company may terminate the agreement at will upon written notice to BioMarin. BioMarin has the right to terminate the agreement upon the Company's bankruptcy or insolvency, or in the event of any challenge or opposition to the licensed patent rights or related actions brought by the Company or its affiliates or sublicensees, or if the Company, its affiliates or sublicensees knowingly assist a third-party in challenging or otherwise opposing the licensed patent rights, except as required under a court order or subpoena.

Agreement with GenStem Therapeutics, Inc. ("GenStem")

On October 2, 2017, the Company entered into a license agreement with GenStem, pursuant to which GenStem granted the Company an exclusive worldwide license, subject to certain retained rights, under certain intellectual property rights owned or controlled by GenStem to develop, commercialize and sell products for use in the treatment of cystinosis. Under this agreement, the Company paid an upfront license fee of $1,000 and is required to make payments upon completion of certain milestones up to an aggregate of $16,000. The next anticipated payment under this Agreement is $2,000, and would become due following the treatment of the first patient in the Phase 1/2 clinical trial of AVR-RD-04 in cystinosis. The Company also agreed to pay GenStem a tiered mid to high single-digit royalty percentage on annual net sales of licensed products as well as a low double-digit percentage of sublicense income received from certain third-party licensees. The Company's royalty obligation expires on a licensed product-by-licensed product and country-by-country basis on the eleventh anniversary of the first commercial sale of such licensed product in such country or the expiration of the last valid claim under the licensed patent rights covering such licensed product in such country, whichever is later. Unless terminated earlier, the agreement expires upon the expiration of the Company's royalty obligation for all licensed products throughout the world. GenStem and the Company can terminate the agreement in the event of a material breach by the other party and failure to cure such breach within a certain period of time. The Company may terminate the agreement at will upon the specified prior written notice to GenStem. No milestone fees related to the license were recorded for the six months ended June 30, 2019 and 2018.

(in thousands, except share and per share data)

Agreement with Lund University Rights Holders

On November 17, 2016, the Company entered into a license agreement with affiliates of Lund University, along with certain other relevant rights holders that may be added from time to time, pursuant to which such rights holders granted to the Company an exclusive worldwide license, subject to certain retained rights, under certain intellectual property rights to develop, commercialize and sell products in any and all uses relevant to Gaucher disease. As consideration for the license, the Company is required to make payments in connection with the achievement of certain milestones up to an aggregate of $550. The agreement expires on the latest of (i) the twentieth anniversary of the end of a certain research project the Company is funding pursuant to an agreement with Lund University, (ii) the expiration of the term of any patent filed on the licensed rights that covers a licensed product, (iii) the expiration of any applicable marketing exclusivity right and (iv) such time that neither the Company nor any sublicensees, partners or contractors are commercializing a licensed product. Either the Company or the rights holders acting together may terminate the license agreement if the other such party commits a material breach and fails to cure such breach within a certain period of time, or if the other party enters into liquidation, becomes insolvent, or enters into composition or statutory reorganization proceedings. No milestone fees related to the license were recorded for the six months ended June 30, 2019 and 2018.

10. Net Loss per Share Attributable to Common Stockholders

For purposes of the diluted net loss per share calculation, stock options, unvested restricted stock, Preferred Stock and the warrant to purchase shares of Series A Preferred Stock are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The following potentially dilutive common stock equivalents, presented based on amounts outstanding at each period end, were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods indicated:

	Six Months Ended June 30,	
	2019	2018
Options to purchase common stock	2,957,457	1,871,139
Restricted common stock	94,065	214,789
Warrants to purchase redeemable convertible preferred stock (as converted to common stock)	—	6,850

11. Commitments and Contingencies

Lease Agreement

On January 12, 2018, the Company entered into a lease agreement for office space located in Cambridge, Massachusetts. The lease agreement expires in January 2023, with a landlord who is an affiliate of the landlord of the Company's prior lease facility. The annual lease payments are subject to a 3% increase each year. The Company recognizes rent expense on a straight-line basis over the lease period and has recorded deferred rent for rent expense incurred but not yet paid. The Company received a tenant incentive allowance of $842 in 2018. Such incentive allowance is being amortized as a reduction of rent expense on a straight-line basis over the lease period. In accordance with the lease agreement, the Company is required to maintain a security deposit of $209, which was recorded in other assets. In contemplation of this agreement, the Company terminated its prior lease agreement.

On August 31, 2018, the Company entered into a sub-lease agreement for lab space located in Cambridge, Massachusetts, United States, which expires in October 2020. The annual lease payments are subject to a 3% increase each year. In accordance with the lease agreement, the Company is required to maintain a security deposit of $283, which was recorded in other assets as of September 30, 2018.

Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the six months ended June 30, 2019 and 2018 and to the best of its knowledge, no material legal proceedings are currently pending or threatened.

Other

The Company is also party to various agreements, principally relating to licensed technology, that require future payments relating to milestones not met at June 30, 2019 and December 31, 2018, or royalties on future sales. No milestone or royalty payments under these agreements are expected to be payable in the immediate future, except as disclosed in Note 9. See Note 9 for discussion of these arrangements.

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third-party with respect to the Company's products. Further, the Company indemnifies its directors and officers who are, or were, serving at the Company's request in such capacities. The Company's maximum exposure under these arrangements is unknown at June 30, 2019. The Company does not anticipate recognizing any significant losses relating to these arrangements. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

12. Related Party Transactions

UHN

In connection with the Company's entry into a license agreement with UHN on January 27, 2016, the Company issued UHN 1,161,665 shares of its common stock. Upon the closing of the IPO, as UHN's fully-diluted percentage ownership of the Company was reduced within a range of specified percentages, the Company was obligated to pay UHN an amount up to $2,000, which was paid in July 2018. See Note 3 for further discussion on the accounting treatment for this provision.

For the three months ended June 30, 2019 and 2018, the Company recognized $132 and zero, respectively, of research and development expense related to the license agreements with UHN (Note 9). For the six months ended June 30, 2019 and 2018, the Company recognized $363 and $41, respectively, of research and development expense related to the license agreements with UHN (Note 9).

Others

For the three and six months ended June 30, 2019, the Company recorded expenses of $365 and $721, respectively, related to a sublease to rent lab space, provided by an entity affiliated with a member of the Board. No such expense was recorded for the three and six months ended June 30, 2018.

For the three and six months ended June 30, 2019 and 2018, the Company recognized zero and $40, respectively, related to consulting services provided by an entity affiliated with an officer of the Company and a member of the Board.

13. Subsequent Events

In July 2019, the Company closed an underwritten public offering of 7,475,000 shares of its common stock at a public offering price of $18.50 per share, which included 975,000 shares of the Company's common stock resulting from the full exercise of the underwriters' option to purchase additional shares at the public offering price, less underwriting discounts and commissions. The net proceeds to the Company from this offering, after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company, were approximately $129,500.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our audited consolidated financial statements and related notes for the year ended December 31, 2018 included in our Annual Report on Form 10-K for the year ended December 31, 2018. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks, uncertainties and assumptions. Factors that might cause future results to differ materially from those projected in the forward-looking statements include, but are not limited to, those set forth in our Annual Report on Form 10-K for the year ended December 31, 2018, as supplemented by our subsequent filings with the SEC.

Overview

We are a Phase 2 clinical stage gene therapy company focused on developing potentially curative *ex vivo* lentiviral-based gene therapies to treat rare diseases following a single dose treatment regimen. Our gene therapies employ hematopoietic stem cells that are harvested from the patient and then modified with lentiviral vectors to insert a functional copy of the gene that is defective in the target disease. We believe that our approach, which is designed to transform stem cells from patients into therapeutic products, has the potential to provide curative benefit for a range of diseases. Our initial focus is on a group of rare genetic diseases referred to as lysosomal storage diseases, which today are primarily managed with enzyme replacement therapies, or ERTs.

Our initial pipeline is comprised of four lentiviral-based gene therapy programs, including AVR-RD-01 for the treatment of Fabry disease, AVR-RD-02 for the treatment of Gaucher disease, AVR-RD-04 for the treatment of cystinosis, and AVR-RD-03 for the treatment of Pompe disease. We are initially targeting rare diseases in which the current standard of care provides the mechanistic proof that the enzymes or proteins produced endogenously following treatment with our gene therapies can offer benefit to patients. Typically, in lysosomal storage diseases, a gene mutation results in the deficiency or malfunctioning of an enzyme or other protein. This results in the inability of lysosomes to properly process cellular byproducts. As a result, these byproducts accumulate to toxic levels in the body's cells and, in turn, disrupt the function of multiple tissues and organs. Fabry disease, Gaucher disease and Pompe disease are primarily managed by bi-weekly, multi-hour infusions with ERTs that seek to exogenously replace the missing enzyme. However, given the characteristics of most ERTs, they typically only remain in the plasma for a short period of time and thus, are not ideal because they are only dosed every two weeks. These existing therapies manage, rather than cure, the underlying diseases and, as a result, patients continue to have disease progression. Further, the frequent, periodic and life-long dosing schedule required for ERTs results in significant costs for the healthcare system and is burdensome for the patient.

We seek to develop promising gene therapy programs by applying our expertise in gene and cellular therapies and clinical and regulatory strategy and execution to efficiently bring these potentially curative therapies to patients. In our initial programs, we leverage years of extensive preclinical and early clinical research by leading international researchers, as well as our internal research efforts, to advance potential therapies. We plan to identify and develop future product candidates through our own internal research efforts as well as through collaborations with leading academics.

We continue our move towards implementing our commercial-scale plato™ platform, including heightened vector efficiency, our closed, automated manufacturing system and utilization of a therapeutic drug monitoring, or TDM, conditioning regimen. These platform improvements have been designed with the intent of improving safety and enhancing the potency and long-term durability of our therapies. We are developing the plato platform to form the backbone of our commercial programs, with the intent of replacing our original academic platform with improved solutions for delivering our gene therapy candidates to patients in multiple disease indications. We believe improvements from our plato platform may lead to better patient outcomes with our gene therapy candidates.

Since our inception in 2015, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights, conducting discovery, research and development activities for our programs and planning for potential commercialization. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations with proceeds from the sales of preferred stock and our initial public offering, or IPO, and an underwritten public offering that closed in July 2019. Through June 30, 2019, we had received gross proceeds of $87.5 million from the sales of our preferred stock and $114.7 million from the sales of common stock through our IPO. In July 2019, we closed an underwritten public offering that raised additional net proceeds of approximately $129.5 million. Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates and programs. Our net losses were $33.2 million and $18.7 million for the six months ended June 30, 2019 and 2018, respectively. As of June 30, 2019 we had an accumulated deficit of $104.9 million. We expect to continue to incur significant expenses for at least the next several years as we advance our product candidates from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates. Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations with proceeds from outside sources, with a majority of such proceeds to be derived from sales of equity, including the net proceeds from our IPO and the underwritten public offering that closed in July 2019. We also plan to pursue additional funding from outside sources, including our expansion of, or our entry into, new borrowing arrangements; research and development incentive payments from the Australian government; and our entry into potential future collaboration agreements for one or more of our programs. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of June 30, 2019, we had cash and cash equivalents of $90.3 million. On July 1, 2019, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by us of up to an aggregate of $200.0 million of our common stock, preferred stock, debt securities, warrants and/or units, which we refer to as the Shelf. We simultaneously entered into a Sales Agreement with Cowen and Company, LLC, as sales agent, to provide for the offering, issuance and sale by the Company of up to $50.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf. The Shelf was declared effective by the SEC on July 10, 2019.

In July 2019, we closed an underwritten public offering under the Shelf of 7,475,000 shares of our common stock at a public offering price of $18.50 per share, which included 975,000 shares of our common stock resulting from the full exercise of the underwriters' option to purchase additional shares at the public offering price, less underwriting discounts and commissions. The net proceeds to us from this offering, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us, were approximately $129.5 million. We believe that our existing cash and cash equivalents as of June 30, 2019, together with the net proceeds from our July 2019 underwritten public offering, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2021. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources." To finance our operations beyond that point, we will need to raise additional capital, which cannot be assured.

Additional Recent Developments

AVR-RD-01 for Fabry disease

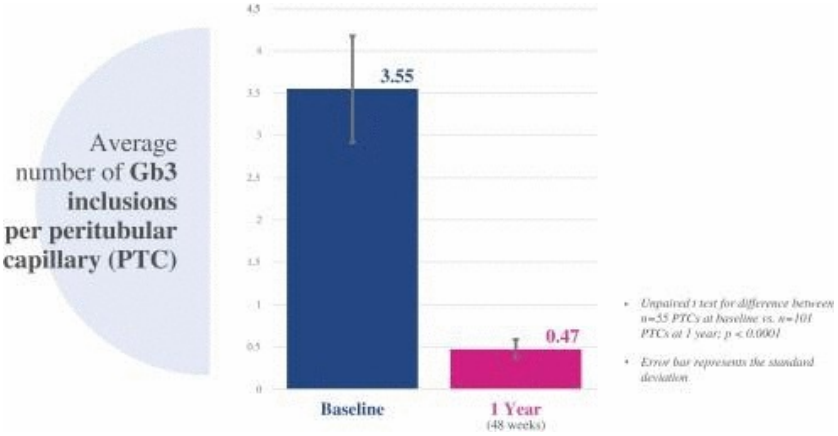
In July 2019, we announced clinical data from clinical trials of our investigational gene therapy AVR-RD-01 in Fabry disease. AVR-RD-01 is currently being studied in two ongoing clinical trials. A Phase 1 investigator-sponsored clinical trial of AVR-RD-01 is being conducted by the University Health Network, or UHN, and sponsored by Fabry Disease Clinical Research and Therapeutics, or FACTs, at three centers in Canada. A total of five patients with Fabry disease who have been previously treated with enzyme replacement therapy, or ERT, for at least six months have been enrolled and enrollment is complete. In addition, we are sponsoring a Phase 2 open-label, multinational clinical trial of AVR-RD-01, with expected enrollment of eight to 12 treatment-naïve males, 16 years and older, with classic Fabry disease, who have not been treated with ERT within 10 years prior to enrollment or chaperone therapy at any time. As of July 15, 2019, three patients in Australia have enrolled in this Phase 2 clinical trial, and we currently have the necessary regulatory clearances to expand enrollment to sites in Canada and the United States.

The primary efficacy endpoint of our Phase 2 clinical trial is the change from baseline in the average number of globotriaosylceramide, or Gb3, inclusions per peritubular capillary, or PTC, as measured in a patient kidney biopsy one year (48 weeks) after treatment with AVR-RD-01. In addition to safety, the Phase 2 and Phase 1 clinical trials are also examining additional secondary efficacy endpoints including biomarkers such as plasma lyso-globotriaosylsphingosine, or lyso-Gb3, alpha-galactosidase A, or AGA, enzyme levels measured in plasma and leukocytes, as well as certain parameters of organ function. In addition, vector copy number, or VCN, is being measured in these trials to assess the potential durability of the gene therapy. Safety and tolerability parameters also are being assessed in these trials.

- ***Kidney biopsy / Gb3 PTC reductions***. The primary efficacy endpoint of our Phase 2 clinical trial is the change, from baseline to one year post-treatment with AVR-RD-01, in the average number of Gb3 inclusions per PTC, as measured in a patient kidney biopsy. Gb3, also referred to as GL-3, is a type of fatty substrate that builds in the cells of Fabry patients, resulting in damage to organs such as kidneys and heart. PTCs, also referred to as kidney interstitial capillaries, or KICs, in Fabry clinical trials, convey blood after filtration in the glomeruli, enabling the blood to eventually exit the kidney and return to the circulatory system.

The first patient in our Phase 2 clinical trial, who had not previously received ERT, exhibited a reduction from an average of 3.55 Gb3 inclusions per PTC at baseline to an average of 0.47 inclusions per PTC one year after administration of AVR-RD-01, representing an 87% reduction and a numerical decrease of 3.08. The following figure illustrates this decrease in average Gb3 inclusions per PTC for this patient.

Phase 2 Patient 1: 87% substrate reduction in kidney biopsy



Baseline: *The last available, non-missing observation prior to AVR-RD-01 infusion*
Note: *With respect to Fabry disease clinical trials, Gb3 inclusions per PTC is interchangeable with GL-3 inclusions per KIC*

- ***Plasma lyso-Gb3 reductions.*** The first patient in our Phase 2 trial (who was treatment-naïve) had an 87% reduction in plasma lyso-Gb3 as of one year after treatment with AVR-RD-01. In addition, in the first four patients in the Phase 1 clinical trial of AVR-RD-01 for whom efficacy data is available at six months or more post-treatment with AVR-RD-01, we observed consistent reductions in plasma lyso-Gb3 levels. In these first four Phase 1 patients, we have observed plasma lyso-Gb3 at levels post-treatment that are lower than the levels observed when the patient received only ERT prior to administration of AVR-RD-01, which we refer to as baseline ERT levels. We define baseline ERT for these Phase 1 patients as the mean of the plasma lyso-Gb3 values reported prior to initiating mobilization. These first four Phase 1 patients exhibited reductions in plasma lyso-Gb3 levels between 33% and 41% compared to their baseline ERT levels.

  The following figures summarize the plasma lyso-Gb3 data observed in the first four patients from the ongoing Phase 1 clinical trial of AVR-RD-01:

Phase 1: Plasma lyso-Gb3 consistently reduced by 33-41% vs. baseline* ERT at 6+ months post-AVR-RD-01 treatment

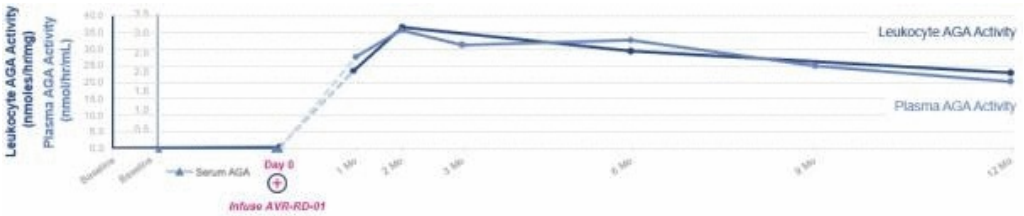
***Baseline**: The mean of the values reported prior to initiating mobilization*
***Percent reduction**: As measured from baseline to last assessment*

Plasma lyso-Gb3 data are also available for Patient 5 in the Phase 1 trial, up to three months post-treatment with AVR-RD-01. This patient's baseline ERT (as defined above) was 15.84 nM, and his plasma lyso-Gb3 levels were 17.8 nM and 14.56 nM at 1 month and 3 months post-treatment with AVR-RD-01, respectively. Plasma lyso-Gb3 data are also available for Patient 2 in the Phase 2 trial, up to six months post-treatment with AVR-RD-01. This patient has an N215S genotype, which is associated with a late-onset cardiac variant phenotype and lower plasma lyso-Gb3 levels. His plasma lyso-Gb3 levels were 7.59 nM, 5.9 nM, 5.8 nM, 5.9 nM, and 6.71 nM at baseline, one month, two months, three months, and six months post-treatment with AVR-RD-01, respectively. This patient's cardiac variant phenotype does not typically result in Gb3 accumulation in the kidney and skin, and accordingly we do not expect that data obtained from this patient will have a meaningful impact on certain efficacy endpoints in our Phase 2 clinical trial, including kidney and skin biopsies. Nonetheless, there may be other important insights derived from data collected from this patient in the Phase 2 clinical trial.

- ***AGA enzyme activity as measured in plasma and leukocytes***. We believe, based on years of observations of Fabry patients prescribed ERT, that even partial plasma AGA activity is associated with improved outcomes in Fabry patients. AGA enzyme activity is able to reduce Gb3 levels in multiple cells and tissues. For our gene therapy, functional AGA is in part produced by the pool of circulating leukocytes derived from genetically-modified CD34+ hematopoietic stem cells, which may directly contribute to clearance of accumulated Gb3 in cells. Functional plasma AGA enters cells and travels to the lysosomes, where it can degrade Gb3. This process is referred to as cross-correction. Genetically-modified leukocytes are the progeny of transduced cells from the gene therapy. As a result, we believe that assessing leukocyte AGA activity provides a potentially improved measure to assess the durability of the gene therapy than plasma AGA enzyme activity alone.

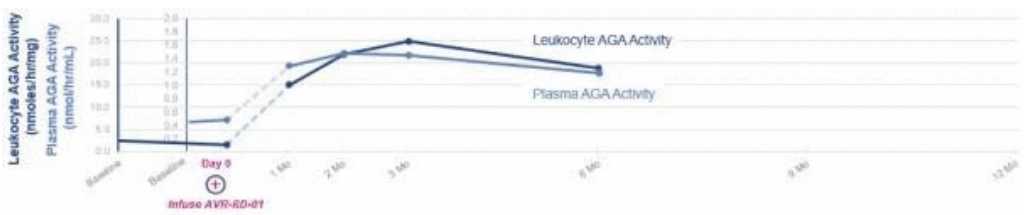
  All six patients in our Phase 2 and Phase 1 clinical trials for whom data are reported at six months or longer post-treatment with AVR-RD-01 (out of a total of eight patients enrolled to date) have exhibited sustained AGA enzyme activity in both the plasma and leukocytes. The following figures summarize the plasma and leukocyte AGA enzyme activity reported from the ongoing clinical trials of AVR-RD-01 as of July 15, 2019.

Phase 2 Patient 1: Sustained leukocyte and plasma enzyme activity at 1 year



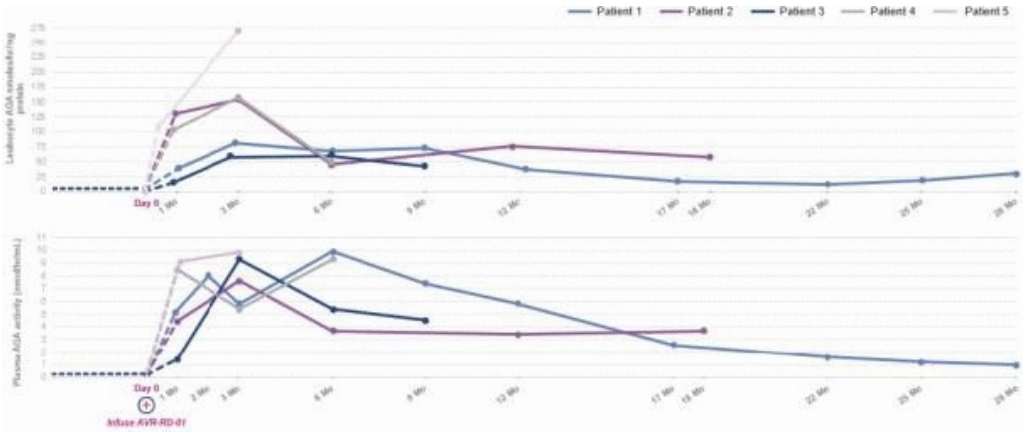
Baseline: *The last available, non-missing observation prior to AVR-RD-01 infusion*

Phase 2 Patient 2: Sustained leukocyte and plasma enzyme activity at 6 months



Note: *Patient 3 had plasma AGA activity of 0.740, leukocyte AGA activity of 9.94 as of 1 month*
Baseline*: The last available, non-missing observation prior to AVR-RD-01 infusion*

Phase 1: Leukocyte and plasma enzyme activity levels trend consistently across all patients



***Note**: Enzyme measurements are taken at ERT troughs; Note: Dotted line illustrative only*
Patient #5's Day 12 data point was utilized since the one month data was not obtained

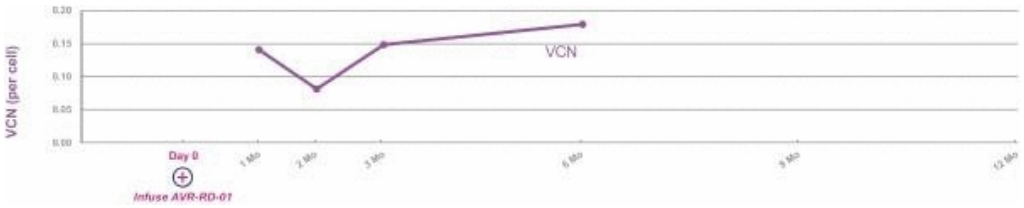
- ***Vector Copy Number.*** Vector Copy Number, or VCN, refers to the average number of copies of the lentiviral-vector inserted gene that are integrated into the genome of a cell, and is another measure that can be used to help assess the durability of a gene therapy. We believe that different diseases may require varying levels of VCN based on the underlying condition, and therefore VCN measurements across different diseases should be assessed separately. For example, a VCN of 0.1 represents 5% to 10% of all nucleated circulating blood cells carrying one to two copies of the inserted gene, which we believe may be sufficient to result in clinically meaningful AGA enzyme activity in the case of Fabry disease, as suggested by our preliminary interim data from our ongoing clinical trials of our investigational gene therapy, AVR-RD-01, in Fabry disease.

  All six patients in our Phase 2 and Phase 1 clinical trials for whom data are reported at six months or longer following administration of AVR-RD-01 have exhibited consistent VCN trends, with VCN levels for the first Phase 1 patient stable at over two years post-treatment. The following figures summarize the VCN observations from the ongoing clinical trials of AVR-RD-01.

Patient 1 in Phase 2 Trial: VCN stable at 1 year

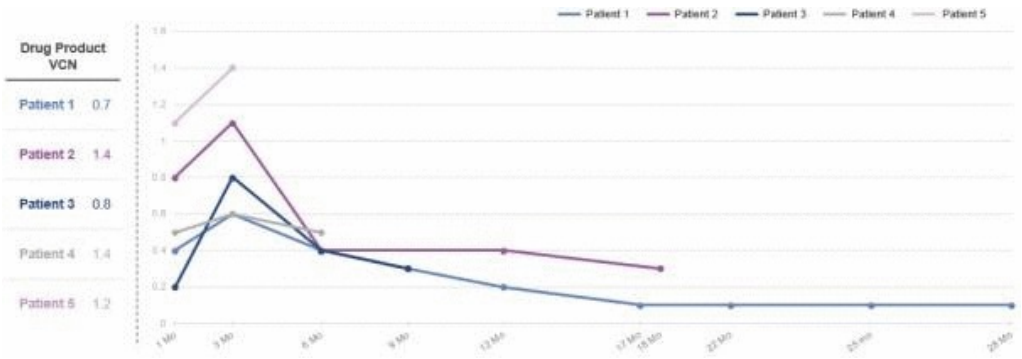
***Note**: 0.1 VCN is indicative of approx. 5-10% of all nucleated circulating blood cells having an average of 1-2 copies of the transgene*

Patient 2 in Phase 2 Trial: VCN at 6 months



***Note**: Patient 3 had VCN of 0.12 as of 1 month*
***Note**: **0.1** VCN is indicative of approx. 5-10% of all nucleated circulating blood cells having an average of 1-2 copies of the transgene*

Phase 1 Trial: Consistent VCN trend across all patients



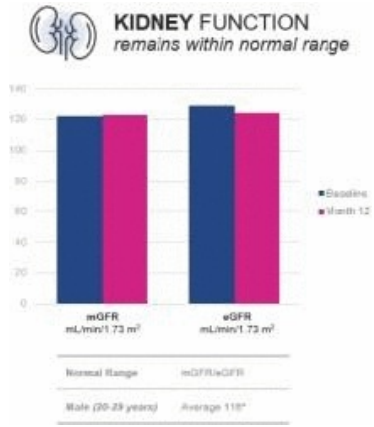
***Note**: 0.1 VCN is indicative of approx. 5-10% of all nucleated circulating blood cells having an average of 1-2 copies of the transgene*

- ***Kidney and cardiac function stability***. Secondary endpoints of our Phase 2 trial include measurements of kidney function, as measured by estimated glomerular filtration rate, or eGFR, and measured glomerular filtration rate, or mGFR, as well as measures of cardiac function, as assessed by Left Ventricular Mass Index, or LVMI. eGFR is determined using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula and mGFR is determined using plasma clearance of iohexol. The left ventricular mass (LVM) is assessed by cardiac magnetic resonance imaging, or cardiac MRI, which is an imaging technology that enables non-invasive assessment of the function and structure of the heart. In general, for a patient with Fabry disease, an increase over time in LVM could potentially be expected. In the case of the first patient in our Phase 2 clinical trial, a 9% reduction in LVM was observed from baseline to one year post-treatment with AVR-RD-01.

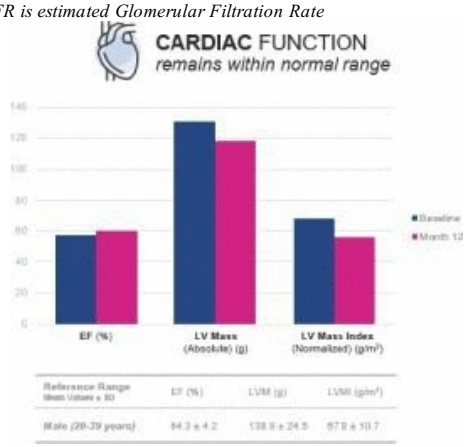
  Halting the progression of organ damage and improving outcomes of patients is a key mission of our Company and our investigational gene therapy programs. Assessment of kidney and cardiac function versus baseline is a secondary efficacy measure in our Phase 2 protocol. Such assessment is not, however, included in the Phase 1 protocol, and therefore such parameters are not discussed for Phase 1.

  As shown below, interim data-to-date in the first patient in our Phase 2 trial indicates kidney and cardiac functions have been stable and in the normal range at one year following administration of AVR-RD-01 investigational gene therapy.

Phase 2 Patient 1: Kidney and cardiac function stable at one year



Source: *https://www.kidney.org/atoz/content/gfr*
Note: *mGFR is measured Glomerular Filtration Rate, eGFR is estimated Glomerular Filtration Rate*



Source: *Alfakih K et al, J Magn Reson Imaging, 2003*
Note: *EF is Ejection Fraction, LVMI is Left Ventricular Mass Index*

- ***ERT Discontinuation by Phase 1 Patients.*** Three patients in the Phase 1 clinical trial who have been treated with AVR-RD-01, our investigational gene therapy, have discontinued ERT and have remained off ERT since such discontinuations. Patient 1 received his last ERT dose in July 2018, Patient 3 received his last ERT dose in May 2018, and Patient 4 received his last ERT dose in June 2019.
- ***Safety Update.*** Interim clinical data for all eight patients dosed to date in the Phase 2 and Phase 1 clinical trials appear to indicate that our AVR-RD-01 investigational gene therapy has been generally well tolerated with no unexpected trends or safety events identified. No serious adverse events, or SAEs, related to the AVR-RD-01 drug product were reported as of the safety data cut-off dates of July 10, 2019 for the Phase 2 trial and May 24, 2019 for the Phase 1 trial. As of the respective safety data cut-off dates, four SAEs were reported in the Phase 2 trial and two SAEs were reported in the Phase 1 trial and were consistent with expectations for the myeloablative conditioning regimen, underlying Fabry disease, or pre-existing conditions.

  In the Phase 2 trial, the four SAEs that were reported through the safety data cut-off date of July 10, 2019 included one report of a Grade 2 pre-treatment seizure experienced after commencing stem cell mobilization but prior to undergoing the conditioning regimen and treatment with AVR-RD-01; one report of Grade 3 dehydration, nausea and vomiting following the conditioning regimen and treatment with AVR-RD-01; and two reports of febrile neutropenia (Grades 3 and 4, respectively) in separate patients following the conditioning regimen and treatment with AVR-RD-01 All four SAEs have subsequently resolved.

In the Phase 1 trial, the two SAEs that were reported through the safety data cut-off date of May 24, 2019 included one report of Grade 3 febrile neutropenia and one report of Grade 2 thrombophlebitis, each occurring following the conditioning regimen and treatment with AVR-RD-01. Both SAEs have subsequently resolved, with the thrombophlebitis SAE verbally reported to the Company as resolved following the safety data cut-off date.

Low anti-AGA antibody titers have been detected in two patients, one in each of the trials, and we believe neither is considered to be of clinical relevance.

Clinical measurements of data, such as AGA enzyme activity and VCN, can provide valuable insight into the potential effectiveness of *ex vivo* CD34+ hematopoietic stem cell gene therapy following administration in a patient. However, such measurements can vary greatly during the initial weeks following administration of the therapy. We believe that the first meaningful measurements of AGA enzyme activity and VCN only start to emerge after 30 to 60 days have passed following administration of the gene-modified CD34+ hematopoietic stem cells. For example, data collected during the early weeks following administration of an *ex vivo* CD34+ hematopoietic stem cell gene therapy may be uninterpretable for reasons such as the manufactured drug product containing a random and indeterminable mixture of cells that may be dominated by late/mature progenitor cells, compared to early progenitor cells and long-term engrafting cells. In such circumstances, the large number of late/mature progenitor cells are over-represented in the collected data in the first few weeks following administration, but are subsequently permanently lost. For these reasons, we have presented in the figures above, and in the future intend to present, AGA enzyme activity data and VCN for patients only after which sufficient time has passed following administration of AVR-RD-01 to allow what we believe to be a meaningful interpretation of results.

Other Pipeline Programs

Our Company-sponsored Phase 1/2 clinical trial evaluating AVR-RD-02 in Gaucher disease, or GAU-201, has commenced active recruitment. The initial clinical site is in Canada and we intend to open additional clinical sites in Australia, the United States and other countries pending regulatory clearances. The first patient in this clinical trial is expected to be dosed in the second half of 2019.

The investigator-sponsored Phase 1/2 clinical trial evaluating AVR-RD-04 in cystinosis has commenced active recruitment. This is a single site investigator-sponsored trial being conducted by our collaborators at the University of California, San Diego, or UCSD. The first patient in this clinical trial is expected to be dosed in the second half of 2019. In June 2019, the UCSD cystinosis study group announced that it had been awarded a grant from the California Institute of Regenerative Medicine, or CIRM, of approximately $12 million to directly fund this phase of the cystinosis clinical trial.

The Pompe disease program is advancing in early pre-clinical development. The IND-enabling pre-clinical program is anticipated to be initiated in 2019.

Plato Platform

Plato is our commercial-stage platform. It is an ex vivo gene therapy platform incorporating multiple recent upgrades including an optimized lentiviral vector, which we refer to as LV2, a closed, automated manufacturing system, and a refined approach to conditioning using busulfan with therapeutic drug monitoring. These three process changes, or upgrades, were recently cleared by applicable regulatory bodies in the United States, Canada and Australia for use in the Phase 2 clinical trial of AVR-RD-01 for Fabry disease and in Canada for the GAU-201 clinical trial of AVR-RD-02 for Gaucher disease. We intend to utilize the plato platform with these process changes for all future patients enrolling in our Phase 2 clinical trial of AVR-RD-01 for Fabry disease and our GAU-201 clinical trial for Gaucher disease.

Components of Our Consolidated Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If development efforts for our product candidates are successful and result in regulatory approval or additional license agreements with third parties, we may generate revenue in the future from product sales.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the discovery and development of our product candidates. We expense research and development costs as incurred. These expenses consist of costs incurred in connection with the development of our product candidates, including:

- license maintenance fees and milestone fees incurred in connection with various license agreements;
- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and commercial materials, including manufacturing validation batches;
- employee-related expenses, including salaries, related benefits, travel and stock-based compensation expense for employees engaged in research and development functions;
- costs related to compliance with regulatory requirements; and
- allocated facilities costs, depreciation and other expenses, which include rent and utilities.

We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers.

Our direct research and development expenses are tracked on a program-by-program basis for our product candidates and consist primarily of external costs, such as fees paid to outside consultants, CROs, CMOs, and central laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct research and development expenses by program also include fees incurred under license agreements. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to oversee the research and discovery as well as for managing our preclinical development, process development, manufacturing and clinical development activities. These employees work across multiple programs and, therefore, we do not track their costs by program.

The table below summarizes our research and development expenses incurred by program (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Fabry	$ 2,336	$ 2,519	$ 4,557	$ 4,407
Gaucher	1,831	1,579	3,897	2,434
Pompe	840	237	2,338	384
Cystinosis	109	129	585	277
AML	—	—	—	46
Unallocated research and development expenses	7,151	2,943	13,336	5,506
Total research and development expenses	$ 12,267	$ 7,407	$ 24,713	$ 13,054

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years, particularly as we increase personnel costs, including stock-based compensation, contractor costs and facilities costs, as we continue to advance the development of our product candidates. We also expect to incur additional expenses related to milestone and royalty payments payable to third parties with whom we have entered into license agreements to acquire the rights to our product candidates.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates or when, if ever, material net cash inflows may commence from any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our preclinical development activities, clinical trials and other research and development activities;
- establishing an appropriate safety profile with IND-enabling studies;
- successful patient enrollment in, and the design, initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials and for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- maintaining a continued acceptable safety profile of the product candidates following approval; and

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the U.S. Food and Drug Administration, or FDA, or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits, travel and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative expenses also include professional fees for legal, consulting, accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We anticipate the additional costs for these services will substantially increase our general and administrative expenses. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and expense as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidate.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on money market funds and other bank deposits.

Other Expense

Other expense consists of foreign exchange gain or loss.

Change in Fair Value of Preferred Stock Warrant Liability

In connection with entering into our loan agreement, we agreed to issue a warrant to purchase shares of our preferred stock to the lender. Prior to the completion of our IPO, we classified the warrant as a liability on our consolidated balance sheet and we were required to remeasure to fair value at each reporting date. We recognized changes in the fair value of the warrant liability as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss. Upon the closing of our IPO, the warrant to purchase preferred stock was converted to a warrant to purchase common stock. The carrying amount of the warrant to purchase preferred stock as of the date of our IPO was transferred to additional paid in capital. No further revaluation is needed for the warrant to purchase common stock.

Change in Fair Value of Derivative Liability

Our stock purchase agreement with University Health Network, or UHN, provided for a payment to UHN upon completion of an initial public offering, which included our IPO, if UHN's fully-diluted percentage ownership of our company was reduced within a range of specified percentages. We classified the IPO dilution payment obligation as a liability on our consolidated balance sheet and we were required to remeasure to fair value at each reporting date. We recognized changes in the fair value of the derivative liability as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss. On June 21, 2018, in connection with our IPO, we remeasured the fair value of the derivative liability to $2.0 million as we were required to pay the dilution payment as mentioned above, which was paid in July 2018.

Consolidated Results of Operations

Comparison of the three months ended June 30, 2019 and 2018

The following table summarizes our consolidated results of operations for the three months ended June 30, 2019 and 2018 (in thousands):

	Three Months Ended June 30,		
	2019	2018	Change
Operating expenses:			
Research and development	$ 12,267	$ 7,407	$ 4,860
General and administrative	4,345	2,140	2,205
Total operating expenses	16,612	9,547	7,065
Loss from operations	(16,612)	(9,547)	(7,065)
Other income (expense):			
Interest income	565	234	331
Change in fair value of preferred stock warrant liability	—	(150)	150
Change in fair value of derivative liability	—	(1,042)	1,042
Other expense	(8)	(2)	(6)
Total other income (expense), net	557	(960)	1,517
Net loss	$ (16,055)	$ (10,507)	$ (5,548)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the three months ended June 30, 2019 and 2018 (in thousands):

	Three Months Ended June 30,		
	2019	2018	Change
Direct research and development expenses by program:			
Fabry	$ 2,336	$ 2,519	$ (183)
Gaucher	1,831	1,579	252
Pompe	840	237	603
Cystinosis	109	129	(20)
AML	—	—	—
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	3,470	2,123	1,347
Other	3,681	820	2,861
Total research and development expenses	$ 12,267	$ 7,407	$ 4,860

Research and development expenses were $12.3 million for the three months ended June 30, 2019, as compared to $7.4 million for the three months ended June 30, 2018. The increase of $4.9 million was primarily due to a decrease of $0.2 million in direct costs related to our Fabry program offset by an increase of $0.3 million in direct costs related to our Gaucher program, an increase of $0.6 million in direct costs related to our Pompe program and an increase of $4.2 million in unallocated research and development costs.

The decrease in direct costs related to our Fabry program was primarily due to a $0.5 million decrease in manufacturing costs partially offset by an increase in clinical costs of $0.2 million and an increase in other costs of $0.2 million.

The increase in direct costs related to our Gaucher program was primarily due to an increase in clinical costs of $0.5 million partially offset by a decrease in preclinical costs of $0.2 million.

The change in direct costs related to our Cystinosis program was less than $0.1 million.

The increase in direct costs related to our Pompe program was primarily due to an increase in preclinical costs of $0.6 million.

The increase in unallocated research and development expenses was primarily due to an increase of $1.3 million in personnel-related costs, including non-cash stock-based compensation, as a result of hiring additional personnel in our research and development department, an increase of $1.0 million in preclinical costs, an increase of $0.7 million in facilities costs and rent expense and an increase of $0.3 million in consulting fees. Personnel-related costs for the three months ended June 30, 2019 and 2018 included non-cash stock-based compensation expense of $0.9 million and $0.3 million, respectively.

General and Administrative Expenses

General and administrative expenses were $4.3 million for the three months ended June 30, 2019, compared to $2.1 million for the three months ended June 30, 2018. The increase of $2.2 million was primarily due to an increase of $1.5 million in personnel-related costs, including non-cash stock-based compensation and an increase of $0.7 million in expenses associated with being a publicly-traded company, including consulting and legal expenses. The increase in personnel-related costs was due to the hiring of additional personnel in our general and administrative functions.

Other Income (Expense), net

Other income (expense), net was income of $0.6 million for the three months ended June 30, 2019, compared to an expense of $1.0 million for the three months ended June 30, 2018. The increase in other income of $1.5 million was primarily due to a $1.1 million expense related to the change in fair value of derivative liability which was recognized during the three months ended June 30, 2018, while no expense related to the change in fair value of derivative liability was recognized during three months ended June 30, 2019, as well as an increase in interest income of $0.3 million during the three months ended June 30, 2019.

Comparison of the six months ended June 30, 2019 and 2018

The following table summarizes our consolidated results of operations for the six months ended June 30, 2019 and 2018 (in thousands):

	Six Months Ended June 30,		
	2019	2018	Change
Operating expenses:			
Research and development	$ 24,713	$ 13,054	$ 11,659
General and administrative	9,599	4,281	5,318
Total operating expenses	34,312	17,335	16,977
Loss from operations	(34,312)	(17,335)	(16,977)
Other income (expense):			
Interest income	1,222	392	830
Change in fair value of preferred stock warrant liability	—	(162)	162
Change in fair value of derivative liability	—	(1,629)	1,629
Other expenses	(68)	(15)	(53)
Total other income (expense), net	1,154	(1,414)	2,568
Net loss	$ (33,158)	$ (18,749)	$ (14,409)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the six months ended June 30, 2019 and 2018 (in thousands):

	Six Months Ended June 30,		
	2019	2018	Change
Direct research and development expenses by program:			
Fabry	$ 4,557	$ 4,407	$ 150
Gaucher	3,897	2,434	1,463
AML	—	46	(46)
Cystinosis	585	277	308
Pompe	2,338	384	1,954
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	6,677	3,743	2,934
Other	6,659	1,763	4,896
Total research and development expenses	$ 24,713	$ 13,054	$ 11,659

Research and development expenses were $24.7 million for the six months ended June 30, 2019, compared to $13.1 million for the six months ended June 30, 2018. The increase of $11.7 million was primarily due to an increase of $0.2 million in direct costs related to our Fabry program, an increase of $1.5 million in direct costs related to our Gaucher program, an increase of $0.3 million in direct costs related to our Cystinosis program, an increase of $2.0 million in direct costs related to our Pompe program and an increase of $7.8 million in unallocated research and development costs.

The increase in direct costs related to our Fabry program was primarily due to an increase of $0.7 million in preclinical and clinical costs partially offset by a decrease of $0.5 million in manufacturing costs.

The increase in direct costs related to our Gaucher program was primarily due to an increase in clinical costs of $0.8 million and an increase of $0.7 million in manufacturing costs.

The increase in direct costs related to our Cystinosis program was primarily due to an increase in preclinical costs of $0.2 million and an increase of $0.1 million in manufacturing costs.

The increase in direct costs related to our Pompe program was primarily due to an increase in preclinical costs of $2.0 million.

The increase in unallocated research and development costs was primarily due to an increase of $2.9 million in personnel-related costs, including non-cash stock-based compensation, as a result of hiring additional personnel in our research and development department, an increase of $1.4 million in preclinical costs, an increase of $1.3 million in facility costs and rent expense, and an increase of $0.4 million in consulting expenses. Personnel-related costs for the six months ended June 30, 2019 and 2018 included non-cash stock-based compensation expense of $1.8 million and $0.3 million, respectively.

General and Administrative Expenses

General and administrative expenses were $9.6 million for the six months ended June 30, 2019, compared to $4.3 million for the six months ended June 30, 2018. The increase of $5.3 million was primarily due to an increase of $2.7 million in personnel-related costs, including non-cash stock-based compensation, an increase of $1.6 million in costs associated with being a publicly-traded company, including consulting, insurance and legal expenses, and an increase of $0.6 million in facilities costs and rent expense.

Other Income (Expense), Net

Other income (expense), net was income of $1.2 million for the six months ended June 30, 2019, compared to an expense of $1.4 million for the six months ended June 30, 2018. The increase in other income (expense) of $2.6 million was primarily due to a $1.6 million expense related to the change in fair value of derivative liability which was recognized during the six months ended June 30, 2018, while no expense related to the change in fair value of derivative liability was recognized during the six months ended June 30, 2019, as well as an increase of $0.8 million in interest income during the six months ended June 30, 2019.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations to date primarily with proceeds from the sale of preferred stock and our common stock through our IPO and our underwritten public offering in July 2019. Through June 30, 2019, we had received gross cash proceeds of $87.5 million and $114.7 million from sales of our preferred stock and IPO, respectively. On July 1, 2019, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by us of up to an aggregate of $200.0 million of our common stock, preferred stock, debt securities, warrants and/or units. We simultaneously entered into a Sales Agreement with Cowen and Company, LLC, as sales agent, to provide for the offering, issuance and sale by the Company of up to $50.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf. The Shelf was declared effective by the SEC on July 10, 2019.

In July 2019, we closed an underwritten public offering under the Shelf of 7,475,000 shares of our common stock at a public offering price of $18.50 per share, which included 975,000 shares of our common stock resulting from the full exercise of the underwriters' option to purchase additional shares at the public offering price, less underwriting discounts and commissions. The net proceeds to us from this offering, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us, were approximately $129.5 million.

Cash in excess of immediate requirements is invested primarily with a view to liquidity and capital preservation.

Cash Flows

The following table summarizes our cash flows for each of the periods presented (in thousands):

	Six Months Ended June 30,	
	2019	2018
Net cash used in operating activities	$ (35,703)	$ (14,229)
Net cash used in investing activities	(741)	(400)
Net cash provided by financing activities	490	163,681
Net (decrease) increase in cash and cash equivalents	$ (35,954)	$ 149,052

Operating Activities

During the six months ended June 30, 2019, operating activities used $35.7 million of cash, cash equivalents and restricted cash, resulting from our net loss of $33.2 million and net cash used by changes in our operating assets and liabilities of $6.0 million, partially offset by non-cash charges of $3.5 million. The net changes in our operating assets and liabilities were primarily due to increases in prepaid expenses and other current assets of $3.8 million due to ongoing preclinical, manufacturing, and clinical trial efforts and decreases in accrued expenses and other current liabilities of $2.1 million. The non-cash charges primarily included $3.1 million of stock-based compensation expense and $0.4 million of depreciation expense.

During the six months ended June 30, 2018, operating activities used $14.2 million of cash, cash equivalents and restricted cash, resulting from our net loss of $18.7 million, partially offset by non-cash charges of $2.7 million and net cash provided by changes in our operating assets and liabilities of $1.9 million. The net changes in our operating assets and liabilities was primarily due to increases in liabilities of $3.0 million due to ongoing research, development, and clinical trial efforts, which were partially offset by increases in assets of $1.2 million, including an increase due to a $0.2 million security deposit for a new lease that was executed in 2018.

Investing Activities

During the six months ended June 30, 2019 and 2018, we used $0.7 million and $0.4 million of cash, cash equivalents and restricted cash, respectively, in investing activities consisting of purchases of property and equipment.

Financing Activities

During the six months ended June 30, 2019, net cash provided by financing activities was $0.5 million, consisting of cash proceeds from exercise of stock options.

During the six months ended June 30, 2018, net cash provided by financing activities was $163.7 million, primarily consisting of net cash proceeds from our issuance of Series B preferred stock in January 2018 and cash proceeds from our issuance of common shares in the IPO in June 2018.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. In addition, we expect to continue to incur additional costs associated with operating as a public company that we had not incurred as a private company. Our expenses will also increase as we:

- continue our development of our product candidates, including continuing enrollment in our ongoing Phase 2 clinical trial for AVR-RD-01, recruitment and activities related to our Phase 1/2 clinical trial for AVR-RD-02, and activities related to the investigator-sponsored Phase 1/2 clinical trial for AVR-RD-04;
- initiate additional clinical trials and preclinical studies for our product candidates;
- seek to identify and develop or in-license or acquire additional product candidates and technologies;
- seek to industrialize our *ex vivo* lentiviral gene therapy approach into a robust, scalable and, if approved, commercially viable process;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- hire and retain additional personnel, such as clinical, quality control, commercial and scientific personnel;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and physical infrastructure to support our research and development; and
- continue to incur additional public company-related costs.

We believe that our existing cash and cash equivalents as of June 30, 2019, together with the net proceeds from our July 2019 underwritten public offering, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2021. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. If we receive regulatory approval for AVR-RD-01 or our other product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, government and other third-party funding, strategic alliances, licensing arrangements or marketing and distribution arrangements. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government and other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The disclosure of our contractual obligations and commitments is set forth under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on March 25, 2019. Except as set forth below, there have been no significant changes to the table contained therein as of June 30, 2019.

Pursuant to our license agreements with UHN, BioMarin, GenStem and the Lund University rights holders, we are required to make certain milestone and royalty payments to our licensors. The next anticipated payment under our license agreement with GenStem is $2 million and would become due following the treatment of the first patient in the Phase 1/2 clinical trial of AVR-RD-04 in cystinosis. The first patient in this clinical trial is expected to be dosed in the second half of 2019.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions. During the six months ended June 30, 2019, there were no material changes to our critical accounting policies. Our critical accounting policies are described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations— Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, which was filed with the SEC on March 25, 2019, and the notes to the consolidated financial statements included in Item 1, "Condensed Consolidated Unaudited Financial Statements," of this Quarterly Report on Form 10-Q.

Emerging Growth Company Status

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. We may take advantage of these exemptions until we are no longer an emerging growth company. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. We have elected to use the extended transition period for complying with new or revised accounting standards and, as a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates. We may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of our IPO or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.07 billion in annual revenue, we have more than $700.0 million in market value of our stock held by non-affiliates (and we have been a public company for at least 12 months and have filed one annual report on Form 10-K) or we issue more than $1.0 billion of non-convertible debt securities over a three-year period.

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 in the rules and regulations of the Securities and Exchange Commission.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing at the beginning of this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

Interest Rate Risk

As of June 30, 2019, we had cash and cash equivalents of $90.3 million, which consisted of cash and money market funds. Interest income is sensitive to changes in the general level of interest rates; however, due to the nature of these investments, an immediate 10% change in interest rates would not have a material impact on our cash and cash equivalents, financial position or results of operations.

Foreign Currency Exchange Risk

We are exposed to foreign exchange rate risk. Our headquarters are located in the United States, where the majority of our general and administrative expenses and research and development costs are incurred in U.S. dollars. A portion of our research and development costs are incurred by our subsidiaries in Australia and Canada, whose functional currencies are the U.S. dollar but engage in transactions in Australian dollars and Canadian dollars, respectively. During each of the three months ended June 30, 2019 and 2018, we recognized foreign currency transaction losses of $8 and $10, respectively. During each of the six months ended June 30, 2019 and 2018, we recognized foreign currency transaction losses of $68 and $15, respectively. These losses primarily related to unrealized and realized foreign currency gains and losses as a result of transactions entered into by our Australian and Canadian subsidiaries in currencies other than the U.S. dollar. These foreign currency transaction gains and losses were recorded in other expense, net in our consolidated statements of operations. We believe that a 10% change in the exchange rate between the U.S. dollar, Australian dollar and Canadian dollar would not have a material impact on our financial position or results of operations.

As we continue to grow our business, our results of operations and cash flows will be subject to fluctuations due to changes in foreign currency exchange rates, which could adversely impact our results of operations. To date, we have not entered into any foreign currency hedging contracts to mitigate our exposure to foreign currency exchange risk.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, 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. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of June 30, 2019, our Chief Executive Officer and Chief Financial Officer concluded that, as a result of the material weaknesses in our internal control over financial reporting as described below and in Part II, Item 1A. of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, our disclosure controls and procedures were not effective as of June 30, 2019. Notwithstanding the material weaknesses, our management has concluded that the financial statements included elsewhere in this report present fairly, in all material respects, our financial position, results of operations, changes in stockholders' equity (deficit) and cash flows in conformity with GAAP.

In connection with the audit of our consolidated financial statements for the years ended December 31, 2017 and 2018, we and our independent registered public accounting firm identified material weaknesses in our internal control over financial reporting related to deficiencies in our controls over the financial statement close and cash disbursement processes. Specifically, there was a lack of controls over the identification and review of complex accounting issues involving significant judgment or estimates as well as the cutoff and classification of certain expenses between general and administrative and research and development. In addition, our internal controls related to the cash disbursements process were not adequately designed to identify unauthorized payment requests. Specifically, in 2017 we were subject to a cyberattack by a third party. This deficiency in our controls resulted in the theft of a portion of our funds.

In 2018, we began implementing measures designed to improve our internal control over financial reporting to remediate these material weaknesses, including formalizing our processes and internal control documentation and strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel and engaging financial consultants to enable the implementation of internal control over financial reporting and segregating duties amongst accounting and finance personnel; and planning to implement certain accounting systems to automate manual processes, such as tracking and accounting for stock-based awards. Although progress has been made to strengthen our controls, management and our independent registered public accounting firm have concluded that the material weaknesses remain unremediated as of December 31, 2018 and June 30, 2019. In addition, in February 2019, one of our vendors was subject to a cyberattack by a third party, which resulted in the payment by us of a fraudulent invoice.

Additionally, in connection with the audit of our consolidated financial statements for the year ended December 31, 2018, we and our independent registered public accounting firm identified a further material weakness in our internal control over financial reporting related to deficiencies in our controls over the financial statement close process. Specifically, there was a lack of controls over the accounting for accrued research and development expenses.

The measures we are implementing are subject to continued management review supported by confirmation and testing, as well as audit committee oversight. Management remains committed to the implementation of remediation efforts to address these material weaknesses. We will continue to implement measures to remedy our internal control deficiencies, though there can be no assurance that our efforts will be successful or avoid potential future material weaknesses. In addition, until remediation steps have been completed and are operated for a sufficient period of time, and subsequent evaluation of their effectiveness is completed, the material weaknesses previously disclosed, and as described above, will continue to exist.

Changes in Internal Control over Financial Reporting

Other than the changes intended to remediate the material weaknesses noted above, no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended June 30, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of June 30, 2019, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this report, including our consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," as well as our other filings with the Securities and Exchange Commission, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties were to occur, which may cause you to lose all or part of the money you paid to buy our common stock. Additional risks that are currently unknown to us or that we currently believe to be immaterial may also impair our business.

Risks related to our financial position and need for additional capital

We have incurred net losses since inception. We expect to incur net losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred net losses. We incurred net losses of $46.4 million and $18.6 million for the years ended December 31, 2018 and 2017, respectively, and $33.2 million for the six months ended June 30, 2019. We historically have financed our operations primarily through private placements of our preferred stock and our initial public offering and follow-on public offering of our common stock. We have devoted substantially all of our efforts to research and development, including clinical and preclinical development of our product candidates, as well as assembling our team. We expect that it will be several years, if ever, before we have commercialized any product candidates. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if, and as, we:

- continue our development of our product candidates, including continuing enrollment in our ongoing Phase 2 clinical trial for AVR-RD-01, recruitment and activities related to our Phase 1/2 clinical trial for AVR-RD-02, and activities related to the investigator-sponsored Phase 1/2 clinical trial for AVR-RD-04;
- advance additional clinical trials and preclinical studies for our product candidates
- seek to identify and develop or in-license additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- continue our implementation of our plato platform as we seek to industrialize our *ex vivo* lentiviral gene therapy approach into a robust, scalable and, if our product candidates are approved, commercially viable process;
- hire and retain additional personnel, such as clinical, quality control, commercial and scientific personnel;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and physical infrastructure to support our research and development; and
- continue to incur additional public company-related costs.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential. This will require us to be successful in a range of challenging activities, and our expenses will increase substantially as we seek to complete preclinical and clinical trials of our product candidates, and manufacture, market and sell these or any future product candidates for which we may obtain marketing approval, if any, and satisfy any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We have never generated revenue from product sales and do not expect to do so for the next several years, if ever.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. We do not anticipate generating revenues from product sales for the next several years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', success in:

- completing research and preclinical and clinical development of our product candidates and identifying new gene therapy product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for adequate coverage and reimbursement by government and third-party payors for our product candidates;
- establishing and maintaining supply and manufacturing processes and relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of our product candidates, if approved, as a viable treatment option;
- addressing any competing technological and market developments;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by FDA or other foreign regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate further clinical trials of and seek marketing approval for, our product candidates and continue to enhance and optimize our vector technology and manufacturing processes. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on reasonable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, laboratory testing, preclinical development and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;

- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs associated with our manufacturing process development and evaluation of third-party manufacturers
- revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms of our current and any future license agreements and collaborations; and
- the extent to which we acquire or in-license other product candidates, technologies and intellectual property.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, will be derived from or based on sales of products that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or cause us to relinquish valuable rights.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity, convertible debt securities or other equity-based derivative securities, your ownership interest will be diluted and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Any additional indebtedness we incur would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline and existing stockholders may not agree with our financing plans or the terms of such financings. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, or our product candidates, or grant licenses on terms unfavorable to us. Adequate additional financing may not be available to us on acceptable terms, or at all.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company founded in November 2015. Our operations to date have been limited to corporate organization, recruiting key personnel, business planning, raising capital, acquiring rights to our technology, identifying potential product candidates, undertaking preclinical studies and planning and supporting clinical trials of our product candidates and establishing research and development and manufacturing capabilities. Although we initiated our ongoing Phase 2 clinical trial for AVR-RD-01 in June 2018, we have not yet demonstrated the ability to complete clinical trials of our product candidates, obtain marketing approvals, manufacture products on a clinical or commercial scale or conduct sales and marketing activities necessary for successful commercialization. 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 new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

Risks related to the discovery and development of our product candidates

Our lentiviral-based gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and of subsequently obtaining regulatory approval.

We have concentrated our research and development efforts on our lentiviral-based gene therapy approach, and our future success depends on our successful development of viable gene therapy product candidates. There can be no assurance that we will not experience problems or delays in developing new product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. For example, the implementation of our plato platform with our planned upgrades, including our transition to TDM conditioning using busulfan for our single-agent conditioning regimen, may result in delays or setbacks in our research and development activities, and we may not realize the intended benefits of these efforts. In addition, we

may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all. For example, we have not yet dosed any patients using our plato platform, which we plan to utilize for the majority of patients in our ongoing Phase 2 clinical trial for AVR-RD-01. The transition to the LV2 lentiviral vector or of our cell processing to an industrialized, automated closed system using disposable supplies may not be successful or may experience unforeseen delays, which may cause shortages or delays in the supply of our products available for clinical trials and future commercial sales, if any, or impair our research and development efforts, including those in our ongoing and future clinical trials. In addition, there is no assurance that products using our proprietary LV2 lentiviral vector or manufactured using this automated system will achieve the same favorable preliminary results observed to date in the Phase 1 and Phase 2 clinical trials of AVR-RD-01.

In addition, the clinical trial requirements of the FDA and other foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied product candidates. To date, only a limited number of gene therapies have received marketing authorization from the FDA or foreign regulatory authorities. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States, Canada or other major markets or how long it will take to commercialize our product candidates, if any are approved. Approvals by foreign regulatory authorities may not be indicative of what the FDA may require for approval, and vice versa.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise the CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or NIH, also are potentially subject to review by the NIH Office of Science Policy's Recombinant DNA Advisory Committee, or the RAC, in limited circumstances. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and authorized its initiation. Conversely, the FDA can put an investigational new drug application, or IND, on clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's institutional biosafety committee, or IBC, as well as its institutional review board, or IRB, would need to review the proposed clinical trial to assess the safety of the trial and may determine that RAC review is needed. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, foreign regulatory authorities may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

The FDA, NIH and the European Medicines Agency, or EMA, have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates.

These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be materially and adversely affected.

The FDA continues to develop its approach to assessing gene and cell therapy products. For example, the agency has released a series of draft guidance documents relating to, among other topics, various aspects of gene therapy product development, review, and approval, including aspects relating to clinical and manufacturing issues related to gene therapy products. We cannot be certain whether such guidance will be relevant to or have an impact on our gene therapy candidates or the duration or expense of any applicable regulatory development and review processes.

Our product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients may experience changes in their health, including illnesses, injuries, discomforts or a fatal outcome. It is possible that as we test AVR-RD-01 or other product candidates in larger, longer and more extensive clinical programs, or as use of our product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier clinical trials, as well as conditions that did not occur or went undetected in previous clinical trials, will be reported by subjects. Gene therapies are also subject to the potential risk that occurrence of adverse events will be delayed following administration of the gene therapy due to persistent biological activity of the genetic material or other components of the vectors used to carry the genetic material. Many times, side effects are only detectable after investigational products are tested in larger scale, pivotal clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that AVR-RD-01 or any other product candidate has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked or limited.

There have been several significant adverse side effects in gene therapy treatments in the past, including multiple reported cases of leukemia, myelodysplastic syndrome and death seen in other clinical trials. Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. Possible adverse side effects that may occur with treatment with gene therapy products include an immunologic reaction early after administration that could substantially limit the effectiveness of the treatment or represent safety risks for patients. Another traditional safety concern for gene therapies using viral vectors has been the possibility of insertional mutagenesis by the vectors, leading to malignant transformation of transduced cells. While our lentiviral gene therapy approach is designed to avoid immunogenicity against the vector after administration, there can be no assurance that patients would not create antibodies that may impair treatment. If any of our gene therapy product candidates demonstrates adverse side effects at unacceptable rates or degrees of severity, we may decide or be required to halt or delay clinical development of such product candidates.

In addition to side effects caused by our product candidates, the conditioning, administration process or related procedures, which we evaluate from time to time as part of our process improvement and optimization efforts, also can cause adverse side effects. A gene therapy patient is generally administered one or more myeloablative drugs to remove stem cells from the bone marrow to create sufficient space in the bone marrow for the modified gene-corrected stem cells to engraft and produce their progeny. This procedure transiently compromises the patient's immune system, known as neutropenia, and ability to form blood clots, known as thrombocytopenia.

We are planning to implement a transition, beginning in the second half of 2019 in connection with our company-sponsored clinical trials, towards a new conditioning regimen for our product candidates utilizing busulfan as the myeloablative conditioning agent instead of the melphalan that is currently used. The use of this conditioning regimen is designed to utilize therapeutic drug monitoring, or TDM, to achieve a balance between the removal of a sufficient amount of bone marrow cells from a patient against potential risks such as toxicity or graft failure. While we anticipate that the conditioning regimen may be performed during a limited hospital stay or potentially through an outpatient procedure on a case-by-case basis as directed by a patient's physician, we cannot guarantee that the conditioning will not require a lengthier hospitalization. Our conditioning regimens may not be successful or may nevertheless result in adverse side effects. For example, in the ongoing investigator-sponsored Phase 1 clinical trial and in the ongoing company-sponsored Phase 2 clinical trial of AVR-RD-01, several serious adverse events, including dehydration, nausea and vomiting, thrombophlebitis, and suppression of neutrophils (febrile neutropenia) following the conditioning process, were reported. While such adverse events in connection with conditioning are expected, if in the future any such adverse events caused by the conditioning process or related procedures continue at unacceptable rates or degrees of severity, the FDA or other foreign regulatory authorities could order us to cease development of, or deny approval of, AVR-RD-01 or our other product candidates for any or all targeted indications. We are aware that there have been cases of therapy-related myelodysplastic syndrome, or t-MDS, a type of blood disorder that is a potential precursor to acute myeloid leukemia, in patients with pre-existing cancer where busulfan treatment was posited to be a contributing factor to this secondary malignancy. However, we have reviewed over 700 published cases of busulfan exposure preceding bone marrow transplant, hematopoietic cell transplant, or ex-vivo gene therapy for non-malignant indications, of which 648 were from peer-reviewed literature. Of the 648 busulfan exposures reported in peer-reviewed literature, none of the cases reported t-MDS. Of the 67 exposures reported in non-peer-reviewed published abstracts, 66 reported no cases of t-MDS resulting from busulfan exposure, and in one case it was reported that a patient developed t-MDS and that busulfan treatment was posited to be a contributing factor. That case has not yet been peer-reviewed, and we believe that due to the presence of other confounding factors in that patient, it has not been conclusively determined that busulfan exposure was the cause of that patient's t-MDS. However, there can be no guarantees that our plan to utilize busulfan in our conditioning regimen will not result in similar adverse events. In addition, although we intend as a precautionary measure to implement new procedures, if and when available, to screen for certain pre-cancerous genetic mutations prior to commencement of the conditioning regimen as an additional risk reduction measure, there can be no guarantees that these procedures will be successful. Even if we are able to demonstrate that adverse events are not product-related, such occurrences could adversely affect patient recruitment or the ability of enrolled patients to complete the clinical trial.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, and restrictions on how or where the product can be distributed, dispensed or used. Furthermore, if we or others later identify undesirable side effects caused by AVR-RD-01 or our other product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such a product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is distributed, dispensed, or administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

AVR-RD-01 is being investigated in an ongoing investigator-sponsored Phase 1 clinical trial and an ongoing company-sponsored Phase 2 clinical trial, and we have not commenced patient dosing in clinical trials for any of our other product candidates. We have never completed a pivotal clinical trial, and may be unable to do so for any product candidates we may develop, including AVR-RD-01.

We are at an early stage of development for all of our product candidates including AVR-RD-01. As of August 1, 2019, our product candidate AVR-RD-01 has been administered only to five patients in an ongoing investigator-sponsored Phase 1 clinical trial and to three patients in our ongoing Phase 2 clinical trial, with dosing dates for the second and third patients in our Phase 2 clinical trial in December 2018 and May 2019, respectively. The ongoing Phase 1 and Phase 2 clinical trials for AVR-RD-01 must be completed, as well as potentially additional pivotal clinical trials, in order to obtain FDA approval to market AVR-RD-01. We have limited experience in preparing, submitting and prosecuting regulatory filings, and have not previously submitted a biologics license application, or BLA, for any product candidate.

Carrying out later-stage clinical trials is a complicated and lengthy process, and we do not expect that all data from patients participating in the clinical trials will be relevant or meaningful. For example, the primary efficacy endpoint of our Phase 2 clinical trial of AVR-RD-01 is the change, from baseline to one year post-treatment with AVR-RD-01, in the average number of Gb3 inclusions per PTC, as measured in a patient kidney biopsy. The second patient in the Phase 2 trial has an N215S genotype, which is associated with a late-onset cardiac variant phenotype and lower plasma lyso-Gb3 levels. This patient's cardiac variant phenotype does not typically result in Gb3 accumulation in the kidney and skin, and accordingly we do not expect that data obtained from this patient will have a meaningful impact on certain efficacy endpoints in our Phase 2 clinical trial, including kidney and skin biopsies. Nonetheless, there may be other important insights derived from data collected from this patient in the Phase 2 clinical trial.

In addition, we have not yet conducted clinical trials of any our product candidates in the United States, and our interactions with the FDA have been limited. We cannot be certain how many additional clinical trials of AVR-RD-01 or any of our other product candidates will be required or how such trials should be designed. In order to commence a clinical trial in the United States, we are required to seek FDA acceptance of an IND for each of our product candidates. We cannot be sure any IND we submit to the FDA, or any similar clinical trial application we submit in other countries, will be accepted. In 2018, we held a pre-IND meeting with the FDA to discuss the requirements to commence clinical trials in the United States. In April 2019, we received clearance from the FDA for the IND application of AVR-RD-01, and we expect to open a U.S. site for our ongoing Phase 2 clinical trial of AVR-RD-01 in the second half of 2019. However, there can be no assurance that we will commence clinical trials in the United States on our expected timeframe or at all. In addition, while we have received clearance from the FDA to commence clinical testing in the United States for AVR-RD-01, there can be no assurance that we will be able to submit and secure similar clearances for any of our other product candidates. We may also be required to conduct additional preclinical testing prior to filing an IND for any of our product candidates, and the results of any such testing may not be positive. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to a BLA submission and approval of AVR-RD-01 or any of our other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing AVR-RD-01.

The ongoing Phase 1 clinical trial of AVR-RD-01 is an investigator-sponsored trial being conducted by University Health Network. In addition, the Phase 1/2 clinical trial of AVR-RD-04 is being conducted by our collaborators at the University of California, San Diego, for which the FDA accepted an IND in December 2018. We do not control the design or administration of investigator-sponsored trials, nor the submission or approval of any IND or foreign equivalent required to conduct these trials, and the investigator-sponsored trials could, depending on the actions of such third parties, jeopardize the validity of the clinical data generated, identify significant concerns with respect to our product candidates that could impact our findings or clinical trials, and adversely affect our ability to obtain marketing approval from the FDA or other applicable regulatory authorities. To the extent the results of this or other investigator-sponsored trials are inconsistent with, or different from, the results of our planned company-sponsored trials or raise concerns regarding our product candidates, the FDA or a foreign regulatory authority may question the results of the company-sponsored trial, or subject such results to greater scrutiny than it otherwise would. In these circumstances, the FDA or such foreign regulatory authorities may require us to obtain and submit additional clinical data, which could delay clinical development or marketing approval of our product candidates. In addition, while investigator-sponsored trials could be useful to inform our own clinical development efforts, there is no guarantee that we will be able to use the data from these trials to form the basis for regulatory approval of our product candidates.

Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.

Results from preclinical studies or early clinical trials are not necessarily predictive of future clinical trial results and are not necessarily indicative of final results. For example, there can be no assurance that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies or clinical trials will be replicated or will continue in ongoing or future studies or trials. Furthermore, preliminary results may not be indicative of the final results of a trial after all data have been collected and analyzed. Based on results observed from ongoing trials of AVR-RD-01, there can be no assurance that increased levels of AGA in patients treated with AVR-RD-01 will be maintained over time. In addition, while three patients from the ongoing investigator-sponsored Phase 1 clinical trial of AVR-RD-01 have discontinued ERT, there can be no assurance that these patients, or others who in the future may discontinue ERT, will remain off ERT. There is a high failure rate for gene therapy and biologic product candidates proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, the design of a pivotal 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. Our company has limited experience in designing and conducting clinical trials and we may be unable to design and execute a clinical trial to support regulatory approval. To date, we have not received definitive guidance from the FDA or other foreign regulatory bodies regarding the necessary endpoints for approval of any of our product candidates, including AVR-RD-01. While we are aware that the FDA utilized an efficacy endpoint based on patients' kidney biopsy in the recent approval of Migalastat for Fabry disease, for which we are also measuring as our primary efficacy endpoint in our ongoing Phase 2 clinical trial of AVR-RD-01, there can be no guarantees that regulatory agencies will permit us to use the same endpoint in connection with further development of AVR-RD-01. Therefore, there are no assurances that the FDA or other foreign regulatory bodies will find the efficacy endpoints we propose in future pivotal trials to be sufficiently validated and clinically meaningful, or that our product candidates will achieve the pre-specified endpoints in future pivotal trials to a degree of statistical significance. We also may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Our AVR-RD-02, AVR-RD-03 and AVR-RD-04 product candidates have not yet been tested in humans. Any of our other product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies. Any such failure would cause us to abandon the product candidate.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate as well as the completion of required follow-up periods. Patients may be unwilling to participate in our gene therapy clinical trials because of negative publicity from adverse events related to the biotechnology or gene therapy fields, competitive clinical trials for similar patient populations, clinical trials in product candidates employing our vectors, the existence of current treatments or for other reasons. In addition, the indications that we are currently targeting and may in the future target are rare diseases, which may limit the pool of patients that may be enrolled in our ongoing or planned clinical trials. The timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed, which could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. For example, in 2017, the ongoing investigator-sponsored Phase 1 clinical trial of AVR-RD-01 encountered delays in the enrollment of patients due to delays in identifying patients for enrollment and the evaluation of information from screened potential trial participants. Patient enrollment and trial completion is affected by factors including the:

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of gene therapy-based approaches to treatment of diseases, including any required pretreatment conditioning regimens;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- availability of genetic testing for potential patients;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

Our current product candidates are being developed to treat rare conditions. We plan to seek initial marketing approvals in the United States, Europe and certain other major markets, including Japan. We may not be able to initiate or continue clinical trials, including our ongoing Phase 2 clinical trial for AVR-RD-01 for which enrollment is ongoing, if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by FDA or other foreign regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- the absence in some countries of established groups with sufficient regulatory expertise for review of gene therapy protocols;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites;

- delays in obtaining required IRB approval at each clinical study site;
- delays in recruiting suitable patients to participate in our clinical studies;
- imposition of a clinical hold by regulatory agencies, after an inspection of our clinical study operations or study sites;
- failure by our CROs, other third parties or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical study sites or patients dropping out of a study;
- the occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues. In addition, if we make changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions, which could delay our clinical development plan or marketing approval for our product candidates. For example, while we are currently utilizing the LV1 version of the lentiviral vector in the ongoing Phase 1 and Phase 2 clinical trials of AVR-RD-01, we plan to transition our AVR-RD-01 lentiviral vectors to an LV2 version in connection with our plato platform implementation. While LV2 is intended to confer improvements in transduction efficiency in viral production, there is no guarantee that we can realize these intended benefits. In addition, the transition from LV1 to LV2 has required (and is anticipated to continue to require) submission of relevant data to the applicable regulatory authorities in connection with certain of our regulatory filings, including our INDs and clinical trial applications, to demonstrate analytic comparability between LV1 and LV2. Our IND application for our planned Phase 2 clinical study of AVR-RD-01 for Fabry disease in the United States, which was cleared by the FDA in April 2019, included data to demonstrate comparability between LV1 and LV2 and a transition to an automated manufacturing platform. In addition, our CTA (including amendments) for our Phase 1/2 clinical study of AVR-RD-02 for Gaucher disease in Canada, for which Health Canada has issued no objection letters, included data utilizing LV2 and our automated manufacturing platform. While these applications included data relating to our LV2 lentiviral vector and our automated manufacturing process, which are elements of our plato platform, and allow us to commence clinical trials incorporating such elements, there can be no assurance that FDA, Health Canada or other regulatory authorities will not require us to undertake additional actions in connection with our transition to our plato platform, including submission of additional comparability studies in connection with future regulatory filings, which may result in delays, suspension or termination of ongoing or future clinical trials, or our inability to conduct our trials according to the plans or the timelines that we have envisioned. For example, the Phase 1/2 investigator-sponsored clinical study of AVR-RD-04 for cystinosis in the United States, which has been cleared by the FDA, does not include our LV2 lentiviral vector or our automated manufacturing platform, and we anticipate that we will be required to submit comparability data in future regulatory filings relating to our transition to LV2 and the automated manufacturing platform. Any such filings may result in delay, suspension or termination of ongoing or future clinical trials pending our submission, and the applicable regulatory agency's review, of such updates. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If the results of our clinical studies are inconclusive or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to changes with the way the product is administered;
- be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a REMS;

- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and impair our ability to commercialize our products.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. If we are unable to obtain necessary regulatory approvals, our business, prospects, financial condition and results of operations may suffer.

Certain of our clinical trials, including the ongoing investigator-sponsored clinical trial of AVR-RD-01, a portion of our Company-sponsored clinical trial of AVR-RD-01, and the investigator-sponsored clinical trial of AVR-RD-04, do not utilize our commercial-scale plato platform. While we have submitted and intend to continue to submit comparability studies to the FDA and other regulatory agencies, as needed, with respect to our transition towards implementing our commercial-scale plato platform, there can be no assurance that the FDA or other regulatory agencies will not in the future require us to conduct additional preclinical studies or clinical trials with respect to these programs or our other product candidates that could result in delays in our development or commercialization programs of our product candidates, if approved, and additional expenses and otherwise could adversely affect our business.

We intend to transition towards implementing our commercial-scale plato platform, including heightened vector efficiency, our closed, automated manufacturing system and utilization of a TDM conditioning regimen, in connection with each of our investigational product candidates. We are developing the plato platform to form the backbone of our commercial programs, with the intent of replacing our original academic platform with improved solutions for delivering our gene therapy candidates to patients in multiple disease indications. We believe improvements from our plato platform may lead to better patient outcomes with our gene therapy candidates. In order to implement this transition, we have been and will be required to conduct additional studies to bridge our modified product candidates to earlier versions, which could delay our clinical development plans or marketing approvals, if any, including for AVR-RD-01, where the ongoing investigator-sponsored clinical trial does not use the plato platform, a portion of our Company-sponsored clinical trial for AVR-RD-01, and for AVR-RD-04 where the planned investigator-sponsored clinical trial will not utilize the plato platform. For example, while we are currently utilizing the LV1 version of the lentiviral vector in the ongoing Phase 1 and Phase 2 clinical trials of AVR-RD-01, we plan to transition our AVR-RD-01 lentiviral vectors to an LV2 version commencing in the second half of 2019. While LV2 is intended to confer improvements in transduction efficiency in viral production, there is no guarantee that we can realize these intended benefits. In addition, the transition from LV1 to LV2 has required (and is anticipated to continue to require) submission of relevant data to the applicable regulatory authorities in connection with certain of our regulatory filings, including our INDs and clinical trial applications, to demonstrate analytic comparability between LV1 and LV2. Our IND application for our planned Phase 2 clinical study of AVR-RD-01 for Fabry disease in the United States, which was cleared by the FDA in April 2019, included data to demonstrate comparability between LV1 and LV2 and a transition to an automated manufacturing platform, which are elements of our plato platform. In addition, our CTA (including amendments) for our planned Phase 1/2 clinical study of AVR-RD-02 for Gaucher disease in Canada, for which Health Canada has issued no objection letters, included data utilizing LV2 and our automated manufacturing platform. Nevertheless, there can be no assurance that the FDA, Health Canada or other regulatory agencies will not in the future require us to conduct additional preclinical studies or clinical trials with respect to these programs or our other product candidates, which may result in delay, suspension or termination of ongoing or future clinical trials. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

While we intend to seek designations for our product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. However, there can be no assurance that we will successfully obtain such designations for any of our product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Breakthrough Therapy Designation for some of our product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA are also eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

In addition, we may seek Fast Track Designation for some of our product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

In addition, we may seek a regenerative medicine advanced therapy, or RMAT, designation for some of our product candidates. An RMAT is defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. A new drug application or a BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a regenerative medicine advanced therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify for RMAT designation, the FDA may later decide that the biological products no longer meet the conditions for qualification.

Outside of the United States, we intend to develop AVR-RD-01 in Japan under the purview of the Japanese Pharmaceutical and Medical Device Agency, or PMDA. Pursuant to Japan's regenerative medicine law, an expedited path to conditional approval may exist for regenerative medicine products that show sufficient safety evidence and signals of efficacy in a Phase 2 clinical trial. However, there can be no assurance that the results of our ongoing Phase 2 clinical trial will demonstrate the safety evidence and efficacy signals required for such conditional approval. In addition, this conditional approval is time-limited, and there must be an agreement as to follow-up collection of information to confirm efficacy and safety, similar to a post-marketing commitment in the United States.

We may be unable to obtain orphan drug designation for our product candidates and, even if we obtain such designation, we may not be able to realize the benefits of such designation, including potential marketing exclusivity of our product candidates, if approved.

Regulatory authorities in some jurisdictions, including the United States and other major markets, may designate drugs intended to treat conditions or diseases affecting relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

If we request orphan drug designation (or the foreign equivalent) for AVR-RD-01 or any of our other product candidates, there can be no assurances that the FDA or foreign regulatory authorities will grant any of our product candidates such designation. In December 2018, the FDA granted our request for orphan drug designation for AVR-RD-01 for the treatment of Fabry disease. To date, we have not obtained orphan drug designation (or the foreign equivalent) for any other product candidates. Additionally, the designation of any of our product candidates as an orphan product does not mean that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or foreign regulatory authorities from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the European Union 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 revoked if any regulatory agency 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 candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition in the United States. Even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory oversight.

Even if we obtain any regulatory approval for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates also may be subject to a REMS, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or CGMP, requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory authority may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise require the withdrawal of the product from the market;
- refuse to permit the import or export of products; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects. In addition, the FDA's policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially and adversely affect our business, financial condition, results of operations and prospects.

We face significant competition in our industry and there can be no assurance that our product candidates, if approved, will achieve acceptance in the market over existing established therapies. In addition, our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our ability to successfully market or commercialize any of our product candidates.

We operate in a highly competitive segment of the biopharmaceutical market. We face competition from many different sources, including larger pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies, some of which are being marketed by large and international companies. In addition, we expect to compete with new treatments that are under development or may be advanced into the clinic by our competitors. There are a variety of product candidates, including gene therapies, in development for the indications that we are targeting.

We anticipate competing with the largest pharmaceutical companies in the world. For example, Sanofi Genzyme and Shire, acquired by Takeda Pharmaceutical Company Ltd., market the enzyme replacement therapies, or ERTs, that represent the standard of care for Fabry patients. Recently, Amicus has secured regulatory approval in the United States and Europe for Migalastat, its oral therapy for Fabry disease. For Gaucher disease, we expect to compete with existing enzyme replacement therapies marketed by Sanofi Genzyme, Shire, Protalix and Pfizer, as well as oral therapies marketed by Actelion and Sanofi. Sanofi also markets an enzyme replacement therapy for Pompe disease. Cystinosis is currently treated by therapies marketed by Horizon Orphan, Mylan, Chiesa, Recordati and Sigma Tau Pharmaceuticals. In addition, we may compete with other gene therapy companies in our industry such as bluebird bio and Spark Therapeutics (which in February 2019 announced that it had entered into an agreement to be acquired by Roche). In particular, a number of gene therapy companies have announced preclinical or clinical adeno-associated virus, or AAV, based gene therapy programs that, if such programs are successful in obtaining regulatory approval, could compete with our gene therapies. These include companies such as Abeona, Amicus, Freeline, Sangamo and uniQure which have announced gene therapy programs for Fabry disease; Freeline and Prevail which have announced gene therapy programs for Gaucher disease; and Abeona, Actus, Amicus, Audentes, Sarepta and Spark Therapeutics which have announced gene therapy programs for Pompe disease.

Many of our competitors have significantly greater financial, product candidate development, manufacturing and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for their products, and mergers and acquisitions within these industries may result in even more resources being concentrated among a smaller number of larger competitors. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the product candidates that we develop obsolete. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our business would be materially and adversely affected if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, have broader market acceptance, are more convenient or are less expensive than any product candidate that we may develop.

Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances.

Our focus on developing our current product candidates may not yield any commercially viable products, and our failure to successfully identify and develop additional product candidates could impair our ability to grow.

As part of our growth strategy, we intend to identify, develop and market additional product candidates beyond our existing product candidates for Fabry disease, Gaucher disease, cystinosis and Pompe disease. We may spend several years completing our development of any particular current or future product candidates, and failure can occur at any stage. The product candidates to which we allocate our resources may not end up being successful. Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential than AVR-RD-01 or our other product candidates. Our spending on current and future research and development programs may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaborations, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate.

Because our internal research capabilities are limited, we may be dependent upon biotechnology companies, academic scientists and other researchers to sell or license product candidates, approved products or the underlying technology to us. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising product candidates and products.

In addition, certain of our current or future product candidates may not demonstrate in patients any or all of the pharmacological benefits we believe they may possess or compare favorably to existing, approved therapies, such as ERT. We have not yet succeeded and may never succeed in demonstrating efficacy and safety of our product candidates or any future product candidates in clinical trials or in obtaining marketing approval thereafter. For example, although we have evaluated AVR-RD-02, AVR-RD-03 and AVR-RD-04 in preclinical studies and have evaluated AVR-RD-01 in ongoing Phase 1 and Phase 2 clinical trials, we have not yet dosed patients in the AVR-RD-02 and AVR-RD-04 clinical trials, nor have we obtained regulatory approval to sell any product based on our therapeutic approaches. Accordingly, our focus on treating these diseases may not result in the development of commercially viable products.

If we are unsuccessful in our development efforts, we may not be able to advance the development of our product candidates, commercialize products, raise capital, expand our business or continue our operations.

Risks related to our reliance on third parties

We expect to rely on third parties to conduct some or all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items. For example, we are moving our cell processing to an automated, closed system with a single third-party supplier.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our preclinical and clinical studies are conducted in accordance with the study plan, protocols and regulatory requirements.

If our contract counterparties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support approval of our product candidates or the FDA or other regulatory agencies may refuse to accept our clinical or preclinical data. For example, in 2017, the ongoing investigator-sponsored Phase 1 clinical trial of AVR-RD-01 encountered delays in the enrollment of patients due to delays in identifying patients for enrollment and the evaluation of information from screened potential trial participants.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to delays of our preclinical and clinical studies or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

We currently have relationships with a limited number of suppliers for the manufacturing of our viral vectors and product candidates. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical studies must be manufactured in accordance with CGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's good laboratory practices, or GLP, and CGMP regulations enforced by the FDA through its facilities inspection program. Some of our contract manufacturers have not produced a commercially-approved product and have never been inspected by the FDA before. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our preclinical and clinical studies may be delayed.

We are dependent on a limited number of suppliers for some of our components and materials used in our product candidates.

We currently depend on a limited number of suppliers for some of the components necessary for our product candidates. We cannot be sure that these suppliers will remain in business, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these materials for our intended purpose. Our use of a limited number of suppliers of raw materials, components and finished goods exposes us to several risks, including disruptions in supply, price increases, late deliveries and an inability to meet customer demand. There are, in general, relatively few alternative sources of supply for these components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any supplier or manufacturing location could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we are required to switch to a replacement supplier, the manufacture and delivery of our product candidates could be interrupted for an extended period, adversely affecting our business. Establishing additional or replacement suppliers may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. For example, the FDA could require additional supplemental data and clinical trial data if we rely upon a new supplier. While we seek to maintain adequate inventory of the components and materials used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to conduct our clinical trials and, if our product candidates are approved, to meet the demand of our customers and cause them to cancel orders. In addition, as part of the FDA's approval of our product candidates, the FDA must review and approve the individual components of our production process, which includes the manufacturing processes and facilities of our suppliers. Our current suppliers have not undergone this process nor have they had any components included in any product approved by the FDA.

Our reliance on these suppliers subjects us to a number of risks that could harm our reputation, business, and financial condition, including, among other things:

- the interruption of supply resulting from modifications to or discontinuation of a supplier's operations;
- delays in product shipments resulting from uncorrected defects, reliability issues, or a supplier's variation in a component;
- a lack of long-term supply arrangements for key components with our suppliers;
- the inability to obtain adequate supply in a timely manner, or to obtain adequate supply on commercially reasonable terms;
- difficulty and cost associated with locating and qualifying alternative suppliers for our components in a timely manner;
- production delays related to the evaluation and testing of products from alternative suppliers, and corresponding regulatory qualifications;
- a delay in delivery due to our suppliers prioritizing other customer orders over ours;
- damage to our reputation caused by defective components produced by our suppliers;
- increased cost of our warranty program due to product repair or replacement based upon defects in components produced by our suppliers; and
- fluctuation in delivery by our suppliers due to changes in demand from us or their other customers.

If any of these risks materialize, costs could significantly increase and our ability to conduct our clinical trials and, if our product candidates are approved, to meet demand for our products could be impacted.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to manufacture our vectors and our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our gene therapy approach, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets.

Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks related to commercialization of our product candidates

If we are unable to establish sales, distribution and marketing capabilities or enter into agreements with third parties to market and sell AVR-RD-01 and our other product candidates, we will be unable to generate any product revenue.

We currently have no sales, distribution or marketing organization. To successfully commercialize any of our current or future product candidates, if approved, we will need to develop these capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any product candidate we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may enter into collaborations regarding any approved product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded sales, distribution and marketing operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates, if approved. Without an internal team or the support of a third-party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.

We focus our research and product development on treatments for serious lysosomal storage diseases. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Even if we obtain any regulatory approval for our product candidates, the commercial success of our product candidates will depend in part on the medical community, patients, and third-party payors accepting gene therapy products in general, and our product candidates in particular, as effective, safe and cost-effective. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of these product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments, including any similar generic treatments;
- the efficacy and safety as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the prevalence and severity of any adverse events or side effects, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects resulting from the conditioning regimen for the administration of our product candidates;
- the ability to offer the products for sale at competitive prices;
- the clinical indications for which the products are approved by the FDA or comparable regulatory agencies;
- the relative convenience and ease of dosing and administration compared to alternative treatments;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- restrictions on how the product is distributed;
- publicity concerning our products or competing products and treatments; and
- favorable third-party insurance coverage and sufficient reimbursement.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments.

Even if a product candidate displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the product, if approved for commercial sale, will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We currently plan to conduct clinical trials for our product candidates outside of the United States, including in Canada, Australia, Japan, Europe and Israel. If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

The insurance coverage and reimbursement status of newly-approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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 might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our or their commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize our product candidates or any other products that we or they may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales 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 health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize our product candidates, if approved. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. 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. Adequate coverage and reimbursement from governmental healthcare programs and commercial payors are critical to new product acceptance. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and certain other major markets where we plan to commercialize may put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems, and 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. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our target patient populations are relatively small, as a result of which the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our product candidates, if approved.

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs or otherwise adversely affect our business.

The manufacturing process we use to produce our product candidates is complex, novel and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we and our manufacturing suppliers employ multiple steps to control the manufacturing process with the goal of ensuring that the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, including even minor deviations from the intended process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA or other applicable regulatory standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Even slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. There is no assurance we will not experience lot failures in the future. Lot failures or product recalls could cause us to delay clinical trials, or, if approved, commercial product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Healthcare legislative reform measures and constraints on national budget social security systems may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in 2010, the Patient Protection and Affordable Care Act or ACA or PPACA, as amended by the Health Care and Education Reconciliation Act of 2010, or the ACA, was enacted, which, substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extends the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjects manufacturers to new annual fees and taxes for certain branded prescription drugs, creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, and provides incentives to programs that increase the federal government's comparative effectiveness research.

Since January 2017, the Trump administration has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. On January 20, 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 burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments asserted to be owed to third-party payors. The effects of this gap in reimbursement on third-party payors, providers, the viability of the ACA marketplace and potentially our business, are not yet known.

Since its enactment, some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, or executive challenges. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. The U.S. Supreme Court has upheld certain key aspects of the legislation, including a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year or pay a penalty, which is commonly known as the "individual mandate." However, as a result of tax reform legislation passed in December 2017, the Tax Cuts and Jobs Act of 2017, or TCJA, the individual mandate has been eliminated effective January 1, 2019. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. The Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal. On July 9, 2019, the U.S. Court of Appeals for the Fifth Circuit held a hearing to determine whether certain states and the House of Representatives have standing to appeal the lower court decision, but it is unclear when the appellate court will render its decision on this hearing, and what effect it will have on the status of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We will continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has recently published a final rule that would give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. Thus, the full impact of the ACA, any law replacing elements of it, and the political uncertainty surrounding any repeal or replacement legislation on our business remains unclear. In addition, other legislative changes have been proposed and adopted in the United States 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. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget for fiscal year 2019 contains further drug price control measures that could be enacted in legislation during 2019 or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately

implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. Finally, on October 25, 2018, CMS issued an Advanced Notice of Proposed Rulemaking, or ANPRM, and is considering issuing a proposed rule in 2019 on a model called the International Pricing Index, or IPI. This model would utilize a basket of other countries' prices as a reference for the Medicare program to use in reimbursing for drugs covered under Part B. The ANPRM also included an updated version of the Competitive Acquisition Program, or CAP, as an alternative to current "buy and bill" payment methods for Part B drugs. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our drug product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any denial in coverage or reduction in reimbursement from Medicare or other government programs may result in a similar denial or reduction in payments from private payors, which may adversely affect our future profitability.

Inadequate funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

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

Any contamination in our manufacturing process, shortages of materials or failure of any of our key suppliers to deliver necessary components could result in interruption in the supply of our product candidates and delays in our clinical development or commercialization schedules.

Given the nature of biologics manufacturing, there is a risk of contamination in our manufacturing processes. Any contamination could materially adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage.

Some of the materials required in our manufacturing process are derived from biologic sources. Such materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Risks related to our business operations

Our gene therapy approach utilizes lentiviral vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with only a limited number of gene therapy products approved to date. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia, myelodysplastic syndromes and deaths seen in other trials using other vectors. Adverse events in our clinical studies, even if not ultimately attributable to our product candidates (such as the many adverse events that typically arise from the conditioning process), or adverse events in other lentiviral gene therapy trials, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team and key employees, including our Chief Executive Officer, Chief Financial Officer, President of Research and Development, Head of Operations, Chief Science Officer, Chief Business Officer, and General Counsel, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. We do not maintain "key person" insurance policies on the lives of these individuals or the lives of any of our other employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

We will need to expand our operations and we may experience difficulties in managing this growth, which could disrupt our operations.

As of June 30, 2019, we had 62 full-time employees. As we mature, we expect to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities and, in the longer term, build a commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA or of other foreign regulatory authorities, provide accurate information to the FDA and other foreign regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or 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, misconduct, 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. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, 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 comply with these 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.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. 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 Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the United States Foreign Corrupt Practices Act's accounting provisions.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws health information privacy and security laws, and other health care laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act, or FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the anti-inducement law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements under the Affordable Care Act, including the provision commonly referred to as the Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payer. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payers, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

The failure to comply with any of these laws or regulatory requirements subjects entities to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in federal and state funded healthcare programs (such as Medicare and Medicaid), contractual damages and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and 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 civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In the event we decide to conduct clinical trials in the European Union, or EU, we may be subject to additional privacy restrictions. The collection and use of personal health data in the EU is governed by the provisions of the General Data Protection Regulation, or GDPR. This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The use of our product candidates in clinical studies and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- the impairment of our business reputation;
- the withdrawal of clinical study participants;
- costs due to related litigation;
- the distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We carry master product liability insurance of $5.0 million per occurrence and $5.0 million in the aggregate in the United States. For Canada, we carry product liability insurance of CAD $10.0 million in the aggregate. For Australia, we carry product liability insurance of AUD $20.0 million in the aggregate. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Patients with the diseases targeted by certain of our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life- threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

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 the success of 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of 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. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although 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 or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business, financial condition, results of operations and prospects.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite our security measures, our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, in 2017 we were subjected to a cyberattack by a third party, which led to the theft of a portion of our funds. We implemented remedial measures promptly following this breach and do not believe that this breach had a material adverse effect on our business. In addition, in February 2019, one of our vendors was subject to a cyberattack by a third party, which resulted in the payment by us of a fraudulent invoice. We are implementing remedial measures following this breach and do not believe that this breach had a material effect on our business. However, if any cyberattack or data breach were to occur in the future and cause interruptions in our or our collaborators', contractors' or consultants' operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials 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 disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the TCJA that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), the limitation of the deduction for net operating losses to 80% of current year taxable income and the elimination of net operating loss carrybacks and modification or repeal of many business deductions and credits (including the reduction of the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). We continue to examine the impact this tax reform legislation may have on our business.

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

As of December 31, 2018, we had federal and state net operating loss carryforwards of $57.3 million and $54.2 million, respectively, and federal and state research and development tax credit carryforwards of approximately $0.3 million and $0.1 million, respectively. If not utilized, the net operating loss carryforwards and research and development credits will generally expire at various dates through 2037. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We may have experienced ownership changes in the past. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurred or occurs and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, it would harm our future operating results by effectively increasing our future tax obligations. Under the TCJA, net operating losses generated after December 31, 2017 will not be subject to expiration.

Risks related to our intellectual property

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and *inter partes* reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we or our licensors are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. In particular, we are aware of issued patents in the United States that cover the lentiviral vectors used in the manufacture of our product candidates. While we believe that we have reasonable defenses against a claim of infringement, potentially including that certain of these patents are expected to expire prior to commercializing our product candidates, if approved, in the United States, there can be no assurance that we will prevail in any such action by the holder of these patents. In the event that the holder of these patents seeks to enforce its patent rights and our defenses against a claim of infringement are unsuccessful, we may not be able to commercialize our product candidates in the United States, if approved, without first obtaining a license to some or all of these patents, which may not be available on commercially reasonable terms or at all. In addition, the defense of any claim of infringement, even if successful, is time-consuming, expensive and diverts the attention of our management from our ongoing business operations.

Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe or be alleged to infringe. In addition, third parties may obtain patents in the future and claim that use of our or our licensors' technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Even in the absence of a finding of infringement, we may choose to obtain a license, if such a license is available. A successful claim of patent or other intellectual property infringement against us could materially adversely affect our business, results of operations and financial condition.

Our rights to develop and commercialize our product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We depend upon the intellectual property rights granted to us under licenses from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. In particular, we have in-licensed certain intellectual property rights and know-how from the University Health Network (relevant to AVR-RD-01 and our Fabry program) and affiliates of Lund University (relevant to AVR-RD-02 and our Gaucher program). In addition, we have in-licensed patents and patent applications from BioMarin Pharmaceutical Inc., or BioMarin (relevant to AVR-RD-03 and our Pompe program), and GenStem Therapeutics, Inc., or GenStem (relevant to AVR-RD-04 and our cystinosis program), directed to compositions and methods related to the manufacture and use of AVR-RD-03 and AVR-RD-04, respectively. Any termination of these licenses could result in the loss of significant rights and could harm or prevent our ability to commercialize our product candidates.

Each of our existing licenses are exclusive but are limited to particular fields, such as Fabry disease, Gaucher disease, Pompe disease, or cystinosis, and are subject to certain retained rights. Absent an amendment or additional agreement, we may not have the right to use intellectual property in-licensed for one of our programs for another program. In addition, licenses that we may enter into in the future may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. For example, pursuant to each of our intellectual property licenses with GenStem, BioMarin, and the rights holders associated with Lund University, our licensors retain control of such activities. Therefore, we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

Our current license agreements impose, and we expect that future license agreements that we may enter into will impose, various obligations, including diligence and certain payment obligations. If we fail to satisfy our obligations, the licensor may have the right to terminate the agreement. Disputes may arise between us and any of our licensors regarding intellectual property subject to such agreements and other issues. Such disputes over intellectual property that we have licensed or the terms of our license agreements may prevent or impair our ability to maintain our current arrangements on acceptable terms, or at all, or may impair the value of the arrangement to us. Any such dispute could have a material adverse effect on our business. If we cannot maintain a necessary license agreement or if the agreement is terminated, we may be unable to successfully develop and commercialize the affected product candidates.

If we are unable to obtain and maintain patent protection for our product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

Our ability to compete effectively will depend, in part, on our ability to maintain the proprietary nature of our technology and manufacturing processes. We rely on manufacturing and other know-how, patents, trade secrets, trademarks, license agreements and contractual provisions to establish our intellectual property rights and protect our products. These legal means, however, afford only limited protection and may not adequately protect our rights. The failure to obtain, maintain, enforce or defend such intellectual property rights, for any reason, could allow third parties to make competing products or impact our ability to develop, manufacture and market our products, if approved, on a commercially viable basis, or at all, which could have a material adverse effect on our financial condition and results of operations.

In particular, we rely primarily on trade secrets, know-how and other unpatented technology, which are difficult to protect. Although we seek such protection in part by entering into confidentiality agreements with our vendors, employees, consultants and others who may have access to proprietary information, we cannot be certain that these agreements will not be breached, adequate remedies for any breach would be available or our trade secrets, know-how and other unpatented proprietary technology will not otherwise become known to or be independently developed by our competitors. If we are unsuccessful in protecting our intellectual property rights, sales of our products may suffer and our ability to generate revenue could be severely impacted.

Our licensors and we have sought, and we intend to continue to seek to protect our proprietary position by filing patent applications in the United States and, in at least some cases, one or more countries outside the United States related to current and future product candidates that are important to our business. However, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents, whether the claims of any issued patents will provide us with a competitive advantage, or whether we will be able to successfully pursue patent applications in the future related to our current or future product candidates. While we have in-licensed patents and patent applications relevant to AVR-RD-03, we currently have no owned or in-licensed patents or patent applications covering AVR-RD-01 or AVR-RD-02, and the patent application that we in-licensed related to AVR-RD-04 is at a very early stage. Many of our product candidates are in-licensed from third parties. Accordingly, in some cases, the availability and scope of potential patent protection is limited based on prior decisions by our licensors or the inventors, such as decisions on when to file patent applications or whether to file patent applications at all.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. Although our license agreements grant us worldwide rights, and our currently in-licensed U.S. patent rights have certain corresponding foreign patents or patent applications, there can be no assurance that we will obtain or maintain such corresponding patents or patent applications with respect to any future license agreements. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States even in jurisdictions where we and our licensors pursue patent protection. Consequently, we and our licensors may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we and our licensors pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we and our licensors have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights, even if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If one of our licensing partners or we initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, should such a patent issue, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Our licensors may face similar risks, which could have an adverse impact on intellectual property that is licensed to us.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

We may be subject to claims challenging the inventorship or ownership of the patents and other intellectual property that we own or license.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an ownership interest in the patents and intellectual property that we own or license or that we may own or license in the future. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own; our licensors may face similar obstacles. We could be subject to ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against any claims challenging inventorship or ownership. If we or our licensors fail in defending any such claims, we may have to pay monetary damages and may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property, which could adversely impact our business, results of operations and financial condition.

Some intellectual property which we have in-licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed, including rights licensed to us by GenStem, may have been generated through the use of U.S. government and California state funding and may therefore be subject to certain federal and state laws and regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply. Any exercise by the government of certain of its rights could harm our competitive position, business, financial condition, results of operations and prospects. With respect to state funding, specifically funding via the California Institute of Regenerative Medicine, or CIRM, the grantee has certain obligations and the state or CIRM has certain rights. For example, the grantee has an obligation to share intellectual property, including research results, generated by CIRM-funded research, for research use in California.

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

Changes in either the patent laws or the interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes several significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a "first-to-invent" system to a "first-to-file" system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and "gene patents" have recently been decided by the Supreme Court of the United States, or Supreme Court. On March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., or Prometheus, a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as "administering" or "determining" steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to not patent-eligible subject matter. On June 13, 2013, the Supreme Court issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc., or Myriad, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent-eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent-eligible. On March 4, 2014, the USPTO issued a guidance memorandum to patent examiners entitled 2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products. These guidelines instruct USPTO examiners on the ramifications of the Prometheus and Myriad rulings and apply the Myriad ruling to natural products and principles including all naturally occurring nucleic acids.

Certain claims of our licensed patents and patent applications contain, and any future patents we may obtain may contain, claims that relate to specific recombinant DNA sequences that are naturally occurring at least in part and, therefore, could be the subject of future challenges made by third parties. In addition, the 2014 USPTO guidance could impact our ability to pursue similar patent claims in patent applications we may prosecute in the future.

We cannot assure you that our efforts to seek patent protection for our product candidates will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in Prometheus and Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent rights and our ability to protect and enforce our intellectual property in the future.

Moreover, although the Supreme Court has held in Myriad that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more U.S. patents that we license or may own or license in the future, if any, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. A patent may only be extended once and only based on a single approved product. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded 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, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. In addition, we do not control the efforts of our licensors to obtain a patent term extension, and there can be no assurance that they will pursue or obtain such extensions to the patents that we license from them.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have a pending trademark application with the USPTO for the mark "plato" but do not have trademarks or trademark applications with the USPTO for the marks "AVROBIO", "AVRO" or the AVROBIO logo. In the future, even if we apply for registration of these marks, there can be no assurance that such registration will be approved. Once registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Intellectual property rights and regulatory exclusivity rights do not necessarily address all potential threats.

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. For example:

- others may be able to make gene therapy products that are similar to our product candidates but that are not covered by the claims of the patents that we license or may own or license in the future;
- we, our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patents or pending patent applications that we license or may own or license in the future;
- we, our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents that we hold rights to or may hold rights to in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- one or more of our product candidates may never be protected by patents;
- 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; and
- we may choose not to file a patent application for certain trade secrets or know-how, and a third party may subsequently file a patent application or obtain a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks related to ownership of our common stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the price at which you purchased our shares.

Our stock price is likely to be volatile. Since our IPO in June 2018, the trading price of our common stock has ranged from $12.46 to $52.70. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which you purchased shares. The market price for our common stock may be influenced by many factors, including:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in other gene therapy products or clinical studies of such products;
- an inability to obtain additional funding;
- failure by us to successfully develop and commercialize our product candidates;
- failure by us to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- an inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- the introduction of new products, services or technologies by our competitors;
- failure by us to meet or exceed financial projections we may provide to the public;
- failure by us to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- the trading volume of our common stock.

In addition, companies trading in the stock market in general, and The Nasdaq Global Select Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

An active trading market for our common stock may not be sustained.

Prior to our initial public offering in June 2018, or our IPO, there had been no public market for our common stock. Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may never be sustained. If an active market for our common stock is not sustained, it may be difficult for you to sell shares you purchased without depressing the market price for the shares, or at all.

An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling additional shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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 will likely 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. Although we have obtained research coverage from certain analysts, there can be no assurance that analysts will continue to cover us or provide favorable 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.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Based on shares outstanding as of August 1, 2019, our executive officers, directors, five percent stockholders and their affiliates beneficially owned approximately 27% of our voting stock. As a result, if these stockholders were to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders. Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current trading price of our stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other stockholders.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the JOBS Act. We will remain an EGC until the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the first day of the year following the first year in which the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, or Section 404;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- an exemption from the requirement to seek nonbinding advisory votes on executive compensation or golden parachute arrangements.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this report. In particular, we have not included in our Form 10-K for the year ended December 31, 2018 or in our 2019 annual proxy statement all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an EGC may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" if the market value of our common stock held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements.

We expect to continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain and maintain director and officer liability insurance.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, and, once we are no longer an EGC or a "smaller reporting company", we will be required to furnish an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, 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 fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock. We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC or a "smaller reporting company", our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five years following the completion of our IPO and will qualify as a "smaller reporting company" if the market value of our common stock held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

We and our independent registered public accounting firm have identified material weaknesses in our internal control over financial reporting. While we have taken numerous steps to address these material weaknesses and believe we have made progress toward remediating them, if we are unable to remedy these material weaknesses, or if we fail to establish and maintain effective internal controls, we may be unable to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective, which could adversely impact our investors' confidence and our stock price.

In connection with the audit of our consolidated financial statements for the years ended December 31, 2016 and 2017, we and our independent registered public accounting firm identified material weaknesses in our internal control over financial reporting related to deficiencies in our controls over the financial statement close and cash disbursement processes. Specifically, there was a lack of controls over the identification and review of complex accounting issues involving significant judgment or estimates as well as the cutoff and classification of certain expenses between general and administrative and research and development. In addition, our internal controls related to the cash disbursements process were not adequately designed to identify unauthorized payment requests. Specifically, in 2017 we were subject to a cyberattack by a third party. This deficiency in our controls resulted in the theft of a portion of our funds.

In 2018, we began implementing measures designed to improve our internal control over financial reporting to remediate these material weaknesses, including formalizing our processes and internal control documentation and strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel and engaging financial consultants to enable the implementation of internal control over financial reporting and segregating duties amongst accounting and finance personnel; and planning to implement certain accounting systems to automate manual processes, such as tracking and accounting for stock-based awards. Although progress has been made to strengthen our controls, as of December 31, 2018, management and our independent registered public accounting firm have concluded that the material weaknesses remain unremediated. In addition, in February 2019, one of our vendors was subject to a cyberattack by a third party, which resulted in the payment by us of a fraudulent invoice.

Additionally, in connection with the audit of our consolidated financial statements for the year ended December 31, 2018, we and our independent registered public accounting firm identified a further material weakness in our internal control over financial reporting related to deficiencies in our controls over the financial statement close process. Specifically, there was a lack of controls over the accounting for accrued research and development expenses.

We expect to incur additional costs to remediate these control deficiencies, though there can be no assurance that our efforts will be successful or avoid potential future material weaknesses. Management remains committed to the implementation of remediation efforts to address these material weaknesses. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, 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.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of August 5, 2019, holders of an aggregate of approximately 5.6 million shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In addition, 2,957,457 shares reserved for issuance upon the exercise of existing stock options outstanding as of June 30, 2019 under our equity incentive plans will become eligible for sale in the public market in the future. We have registered all shares of common stock that we may issue under our equity compensation plans, which can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. For example, our prior loan facility with Silicon Valley Bank restricted our ability to pay any dividends or making any distributions on account of our capital stock, and we may enter into agreements in the future with similar restrictions. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by-laws, include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our bylaws contain exclusive forum provisions, which may limit a stockholder's ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of or based on a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (3) any action asserting a claim against us or any of our current or former directors, officers, employees or stockholders arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act of 1933, as amended (the "Securities Act") or the Securities Exchange Act of 1934. Our amended and restated bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). We have chosen the United States District Court for the District of Massachusetts as the sole and exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision.

On December 19, 2018, in *Sciabacucchi v. Salzberg*, C.A. No. 2017-0931-JTL (Del. Ch.), the Court of Chancery of the State of Delaware issued a decision declaring that federal forum selection provisions that purport to require claims under the Securities Act be brought in federal court are ineffective and invalid under Delaware law. On January 17, 2019, the decision was appealed to the Delaware Supreme Court. While the Delaware Supreme Court dismissed the appeal on jurisdictional grounds, we expect that the appeal will be re-filed once the Court of Chancery issues a final judgment. Unless and until the Court of Chancery's decision in *Sciabacucchi* is reversed by the Delaware Supreme Court or otherwise abrogated, we do not intend to enforce our Federal Forum Provision designating the District of Massachusetts as the exclusive forum for Securities Act claims. In the event that the Delaware Supreme Court affirms the Court of Chancery's *Sciabacucchi* decision or otherwise makes a determination that provisions such as the Federal Forum Provision are invalid, our Board of Directors intends to amend promptly our bylaws to remove the Federal Forum Provision. Such amendment could cause us to incur additional costs, which could have an adverse effect on our business, financial condition or results of operations.

We recognize that the Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, these forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

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

On June 25, 2018, we completed our initial public offering of 6,035,151 shares of our common stock at a price of $19.00 per share for an aggregate offering price of approximately $114.7 million, including the full exercise of the underwriters' option to purchase additional shares. Morgan Stanley & Co. LLC, Cowen and Company, LLC, Wells Fargo Securities, LLC and Wedbush Securities Inc. served as the underwriters of the IPO. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File Nos. 333-225213 and 333-225764), which became effective on June 20, 2018.

We received aggregate net proceeds from the offering of approximately $104.0 million, after deducting underwriting discounts and commissions, as well as other offering expenses. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of June 30, 2019, we had used approximately $64.7 million of the net proceeds from the IPO, primarily to fund our current programs in Fabry disease, Gaucher disease, cystinosis, and Pompe disease; our external and internal manufacturing and process development activities related to our programs and to fund research and development activities that relate to all of our clinical and preclinical activities, including the cost of research and development personnel; and general and administrative expenses, working capital and other general corporate purposes. There has been no material change in our planned use of the net proceeds from the offering as described in the final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act.

Item 3. Defaults Upon Senior Securities.

Not Applicable

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

None

Item 6. Exhibits.

Exhibit Number	Description
3.1	Fourth Amended and Restated Certificate of Incorporation of the Registrant (filed as Exhibit 3.1 to our Current Report on Form 8-K filed on June 25, 2018 and incorporated herein by reference).
3.2	Amended and Restated By-laws (filed as Exhibit 3.2 to our Current Report on Form 8-K filed on June 25, 2018 and incorporated herein by reference).
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Indicates the exhibit is being furnished, not filed, with this report.

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.

AVROBIO, INC.

Date: August 8, 2019

By: /s/ Geoff MacKay

Geoff MacKay

President, Chief Executive Officer, and Principal Executive Officer

Date: August 8, 2019

By: /s/ Erik Ostrowski

Erik Ostrowski

Chief Financial Officer and Principal Financial and Accounting Officer

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Geoff MacKay, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVROBIO, Inc.;

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

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

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

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

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

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

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

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

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

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

Date: August 8, 2019

By: /s/ Geoff MacKay

Geoff MacKay
Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Erik Ostrowski, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVROBIO, Inc.;

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

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

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

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

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

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

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

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

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

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

Date: August 8, 2019

By: /s/ Erik Ostrowski

Erik Ostrowski
Chief Financial Officer

Exhibit 32.1

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

In connection with the Quarterly Report of AVROBIO, Inc. (the "Company") on Form 10-Q for the period ending June 30, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to the best of his or her knowledge that:

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

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

Date: August 8, 2019 By: /s/ Geoff MacKay

Geoff MacKay
Chief Executive Officer

Date: August 8, 2019 By: /s/ Erik Ostrowski

Erik Ostrowski
Chief Financial Officer