HISTOGENICS CORP
Form 10-Q
November 08, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended September 30, 2018

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number 001-36751

Histogenics Corporation

(Exact Name of Registrant as Specified in its Charter)

Delaware	04-3522315
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
830 Winter Street, 3rd Floor	
Waltham, Massachusetts	02451
(Address of principal executive offices)	(Zip Code)

(781) 547-7900

(Registrant's telephone number, including area code)

Not Applicable

(Former name, former address and former fiscal year, if changed since last report)

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 7(a)(2)(B) of the Securities Act.

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

As of November 6, 2018, there were 62,025,398 outstanding shares of the registrant's common stock, $0.01 par value per share.

HISTOGENICS CORPORATION

QUARTERLY REPORT ON FORM 10-Q

FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2018

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

As used in this Quarterly Report on Form 10-Q, the terms “Histogenics,” “Company,” “registrant,” “we,” “us,” and “our” mean Histogenics Corporation and its subsidiaries unless the context indicates otherwise. This Quarterly Report on Form 10-Q contains “forward-looking statements” that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including statements regarding our future results of operations and financial position, strategy and plans, and our expectations for future operations, are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words “anticipate,” “believe,” “contemplates,” “continue,” “could,” “design,” “estimate,” “expect,” “intend,” “likely,” “may,” “ongoing,” “plan,” “potential,” “predict,” “proje “seek,” “should,” “target,” or the negative version of these words and similar expressions are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- expectations regarding the timing and success of discussions with the U.S. Food and Drug Administration (FDA) regarding the submission of a Biologics License Application (BLA) for NeoCart to the FDA;
- the ability to obtain and maintain regulatory approval of our product candidates and the labeling for any approved products, including the timing of a submission of a BLA to the FDA, the FDA’s response to such submission and any requirement by the FDA to complete additional clinical trials or supply other data in advance of any approval;
- our need for additional financing, our ability to raise additional funds on commercially reasonable terms and our ability to obtain stockholder approval to increase authorized shares as our ability to raise capital through the issuance of additional shares of our common stock or convertible securities is restricted by the limited number of our residual authorized shares of common stock;
- our expectations regarding our expenses and revenues, the sufficiency of our cash resources, the timing of our future profitability, if at all;
- the scope, progress and costs of developing and commercializing NeoCart or any future product candidates;
- our ability to establish and maintain development and commercialization partnerships;
- our ability to adequately manufacture our product candidates and the raw materials utilized therein;
- our technology, manufacturing capacity, location and partners;
- the rate and degree of reimbursement and market acceptance of any of our product candidates;
- our expectations regarding competition, including the actions of competitors and the perceived relative performance in the marketplace of NeoCart as compared to competitive products;
- the size and growth of the potential markets for our product candidates, our ability to serve those markets and our ability to gain market share;
- our ability to manufacture our product candidates at an acceptable cost and scale to serve those markets;
- our ability to obtain and maintain intellectual property protection for our product candidates and our cell therapy technology platform;
- the timing and success of preclinical studies and clinical trials conducted by us or our development partners, including the timing of commencement, enrollment, completion and regulatory filings;
- updated or refined data based on continuing review and quality control analysis of clinical data, including the NeoCart Phase 3 clinical trial data;
- our anticipated growth strategies;
- our securities’ or industry analysts’ expectations regarding the commercial success of NeoCart, if approved, and the timing and success of any clinical trials we may initiate in the future;
- the anticipated trends and challenges in our business and the market in which we operate;
- our ability to attract and retain key personnel;
- regulatory developments in the United States and foreign countries; and
- our plans for the use of our cash and cash equivalents.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may

cause actual results to differ materially from current expectations include, among other things, those described in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this Quarterly Report on Form 10-Q and those described in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission on March 15,

2018. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We specifically disclaim any obligation to update these forward-looking statements in the future, except as required by law.

HISTOGENICS (and design), our logo design and NEOCART are our registered trademarks, and BIOCART is our trademark. Any other trademarks, registered marks and trade names appearing in this Quarterly Report on Form 10-Q are the property of their respective holders. All other trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

HISTOGENICS CORPORATION

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share data)

	September 30, 2018 (Unaudited)	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 5,192	$7,081
Marketable securities	—	900
Prepaid expenses and other current assets	825	194
Total current assets	6,017	8,175
Property and equipment, net	4,352	2,723
Other assets, long-term	375	—
Restricted cash	137	137
Total assets	$ 10,881	$11,035
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 1,690	$776
Accrued expenses	1,973	2,705
Current portion of deferred revenue	5,000	—
Current portion of deferred rent	42	35
Current portion of deferred lease incentive	238	111
Current portion of equipment loan	—	178
Total current liabilities	8,943	3,805
Accrued expenses due to Intrexon Corporation	3,040	3,040
Deferred revenue, net of current portion	5,000	—
Deferred rent, net of current portion	334	280
Deferred lease incentive, net of current portion	1,085	499
Warrant liability	2,155	14,679
Total liabilities	20,557	22,303
Commitments and contingencies (Note 5)		
Convertible preferred stock and stockholders' equity (deficit):		
Convertible preferred stock, $0.01 par value; 30,000 shares authorized, 400.4910 and 4,605.6533 shares issued and outstanding at September 30, 2018 and December 31, 2017, respectively	—	—
Common stock, $0.01 par value; 100,000,000 shares authorized, 35,002,742 and	221	159

24,571,029 shares issued and outstanding at September 30, 2018 and December 31, 2017, respectively		
Additional paid-in capital	206,115	196,760
Accumulated deficit	(216,012)	(208,187)
Total stockholders' deficit	(9,676)	(11,268)
Total liabilities and stockholders' deficit	$ 10,881	$11,035

See accompanying notes to unaudited consolidated financial statements.

HISTOGENICS CORPORATION

CONSOLIDATED STATEMENTS OF OPERATIONS

(unaudited)

(in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Revenue	$—	$—	$—	$—
Operating expenses:				
Research and development	4,563	3,488	12,307	12,200
General and administrative	2,426	2,225	8,059	6,717
Total operating expenses	6,989	5,713	20,366	18,917
Loss from operations	(6,989)	(5,713)	(20,366)	(18,917)
Other income (expense):				
Interest income, net	19	39	88	114
Other expense, net	(21)	(52)	(71)	(142)
Change in fair value of warrant liability	17,776	(269)	12,524	(673)
Total other income (expense), net	17,774	(282)	12,541	(701)
Net income (loss)	$10,785	$(5,995)	$(7,825)	$(19,618)
Other comprehensive income (loss):				
Unrealized gain from available for sale securities	—	1	—	—
Comprehensive income (loss)	$10,785	$(5,994)	$(7,825)	$(19,618)
Net income (loss) attributable to common stockholders—basic	$10,650	$(5,080)	$(7,657)	$(16,380)
Net (loss) attributable to common stockholders—diluted	$(7,126)	$(5,080)	$(20,181)	$(16,380)
Net income (loss) per common share—basic	$0.36	$(0.23)	$(0.27)	$(0.74)
Net loss per common share—diluted	$(0.24)	$(0.23)	$(0.68)	$(0.74)
Weighted-average shares used to compute income (loss) per common share—basic	29,737,632	22,552,341	28,723,500	22,219,666
Weighted-average shares used to compute income (loss) per common share—diluted	29,737,632	22,552,341	29,515,700	22,219,666

See accompanying notes to unaudited consolidated financial statements.

HISTOGENICS CORPORATION

CONSOLIDATED STATEMENTS OF CASH FLOWS

(unaudited)

(in thousands)

	Nine Months Ended September 30,	
	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$(7,825)	$(19,618)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	364	1,178
Amortization of discount of investments	—	24
Deferred rent and lease incentive	774	(407)
Stock-based compensation	1,249	1,233
Change in fair value of warrant	(12,524)	673
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(631)	(85)
Other assets, long-term	(375)	—
Accounts payable	861	(761)
Accounts payable due to Intrexon Corporation	—	(360)
Accrued expenses	(732)	(578)
Deferred revenue	10,000	—
Net cash used in operating activities	(8,839)	(18,701)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(1,940)	(132)
Proceeds from maturities of marketable securities	900	6,159
Purchases of marketable securities	—	(8,004)
Net cash used in investing activities	(1,040)	(1,977)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayments on equipment term loan	(178)	(437)
Net proceeds from issuance of common stock	8,164	—
Proceeds from exercise of warrants	2	—
Proceeds from exercise of stock options	2	5
Net cash provided by (used in) financing activities	7,990	(432)
Net decrease in cash and cash equivalents and restricted cash	(1,889)	(21,110)
Cash and cash equivalents and restricted cash—Beginning of period	7,218	32,045
Cash and cash equivalents and restricted cash—End of period	$5,329	$10,935
Supplemental cash flow disclosures from investing and financing activities:		
Purchases of property and equipment in accounts payable and accrued expenses	$53	$—
Public offering costs in accounts payable and accrued expenses	$160	$—

See accompanying notes to unaudited consolidated financial statements

HISTOGENICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(unaudited)

1. NATURE OF BUSINESS

Organization

Histogenics Corporation (the "Company") was incorporated under the laws of the Commonwealth of Massachusetts on June 28, 2000 and has its principal operations in Waltham, Massachusetts. In 2006, the Company's board of directors approved a corporate reorganization pursuant to which the Company incorporated as a Delaware corporation. The Company is a leader in the development of restorative cell therapies ("RCTs"). RCTs refer to a new class of products the Company is developing that are designed to offer patients rapid-onset pain relief and restored function through the repair of damaged or worn tissue. NeoCart, the Company's lead investigational product, is an innovative cell therapy that utilizes various aspects of the Company's RCT technology platform to treat tissue injury in the field of orthopedics, specifically cartilage damage in the knee. NeoCart is designed to rebuild a patient's own knee cartilage to treat pain at the source, improve function and potentially prevent a patient's progression to osteoarthritis. NeoCart is one of the most rigorously studied restorative cell therapies for orthopedic use and is currently in a 249 patient, Phase 3 clinical trial in the United States (the "U.S.") under a special protocol assessment with the U.S. Food and Drug Administration (the "FDA"). In the third quarter of 2018, the Company announced that its Phase 3 clinical trial of NeoCart did not meet the primary endpoint of a statistically significant improvement in pain and function in a dual threshold responder analysis one year after treatment as compared to microfracture. However, NeoCart did demonstrate statistically significant and clinically meaningful improvements on the dual threshold responder analysis six months after treatment and on nearly all individual pain and function measures when compared to microfracture one and two years after treatment. As a result, the Company met with the FDA on October 30, 2018 to discuss the data and a potential Biologics License Application ("BLA") submission. The FDA has not made a final decision regarding a potential BLA submission. The Company and the FDA are continuing to discuss the clinical data generated to date, the potential need for any additional supplemental clinical data (which may include longer-term data from the ongoing Phase 3 clinical trial or additional studies) and potential alternative regulatory pathways for the BLA to be accepted.

On December 18, 2014, the Company formed a wholly owned subsidiary, Histogenics Securities Corporation, under the laws of the Commonwealth of Massachusetts.

On September 29, 2016, the Company closed a private placement of common stock, preferred stock and warrants, contemplated by a securities purchase agreement dated September 15, 2016, with certain institutional and accredited investors. The net proceeds after deducting placement agent fees and other transaction-related expenses was $27.6 million. See Note 6, Capital Stock, for further discussion of the private placement.

In January 2018, the Company completed an underwritten registered direct offering of 2,691,494 shares of common stock. The total net proceeds of the offering were $5.7 million after deducting underwriter's discounts and commissions, and expenses related to the offering.

In March 2018, the Company entered into an equity distribution agreement ("ATM Agreement") with Canaccord Genuity Inc. ("Canaccord"), pursuant to which the Company may, from time to time, sell shares of its common stock having an aggregate offering price of up to $10.0 million (the "Shares") through Canaccord, as sales agent. During the nine months ended September 30, 2018, the Company sold an aggregate of 5,766,247 shares of common stock and received $4.0 million after deducting commissions related to the ATM Agreement and other offering costs. From October 1, 2018 through November 6, 2018, the Company sold an aggregate of 867,656 shares of its common stock and received $0.5 million after deducting commissions related to the ATM Agreement.

On October 10, 2018, the Company closed an underwritten public offering of 26,155,000 shares of its common stock and warrants to purchase up to 19,616,250 shares of common stock, at a combined purchase price of $0.65 per share of common stock and accompanying warrant. The gross proceeds from this offering were $17.0 million, before deducting underwriting discounts and commissions, and offering expenses payable by the Company. The warrants are exercisable immediately upon issuance at a price of $0.70 per share of common stock and have a term of five years commencing on the date of issuance.

Since its inception, the Company has devoted substantially all of its efforts to product development, recruiting management and technical staff, raising capital, starting up production and building infrastructure and has not yet generated revenues from its planned principal operations. Expenses have primarily been for research and development and related administrative costs.

The Company is subject to a number of risks. The developmental nature of its activities is such that significant inherent risks exist in the Company’s operations. Principal among these risks are the successful development of therapeutics, ability to obtain adequate financing, obtaining regulatory approval for any of its product candidates in any jurisdiction, obtaining adequate reimbursement rates for any of its approved product candidates, compliance with government regulations, protection of proprietary therapeutics, fluctuations in operating results, dependence on key personnel and collaborative partners, adoption of the Company’s products by the physician community, rapid technological changes inherent in the markets targeted, the introduction of substitute products and competition from larger companies.

Liquidity

The consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As shown in the accompanying consolidated financial statements, the Company had an accumulated deficit at September 30, 2018 of $216.0 million and has incurred losses and cash flow deficits from operations for the nine months ended September 30, 2018 and 2017. The Company has financed operations to date primarily through public and private placements of equity securities, and borrowings under debt agreements. The Company anticipates that it will continue to incur net losses for the next several years. The Company believes that its existing cash, cash equivalents and marketable securities will only be sufficient to fund its projected cash needs into the middle of 2019. Accordingly, these factors, among others, raise substantial doubt about the Company's ability to continue as a going concern. The Company will require additional capital to sustain operations through FDA approval of NeoCart and to commercialize NeoCart, if approved. To meet its capital needs, the Company intends to raise additional capital through debt or equity financing or other strategic transactions. However, such financing may not be on favorable terms or available to the Company. The failure of the Company to obtain sufficient funds on commercially acceptable terms when needed will have a material adverse effect on the Company's business, results of operations and financial condition. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. The Company has based its estimates on assumptions that may prove to be wrong, and the Company's expenses could prove to be significantly higher than it currently anticipates.

Basis of Accounting

The consolidated financial statements are unaudited and have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). However, they do not include all of the information and footnotes required by GAAP for complete financial statements. These interim consolidated financial statements, in the opinion of the Company's management, reflect all normal recurring adjustments necessary for a fair presentation of the Company's financial position and results of operations for the interim periods ended September 30, 2018 and 2017. The results of operations for the interim periods are not necessarily indicative of the results of operations to be expected for the full year. These interim financial statements should be read in conjunction with the audited financial statements as of and for the year ended December 31, 2017, and the notes thereto, which are included in the Company's Annual Report on Form 10-K, filed with the Securities and Exchange Commission (the "SEC") on March 15, 2018.

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, ProChon and Histogenics Securities Corporation. All significant intercompany accounts and transactions are eliminated in consolidation.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

During the nine months ended September 30, 2018, there have been no material changes to the significant accounting policies described in the Company's audited financial statements as of and for the year ended December 31, 2017, and the notes thereto, which are included in the Annual Report on Form 10-K, except as noted below.

Fair Value Measurements

The carrying amounts reported in the Company's consolidated financial statements for cash and cash equivalents, marketable securities, accounts payable, equipment loan, and accrued liabilities approximate their respective fair values because of the short-term nature of these accounts.

Fair value is defined as the price that would be received if selling an asset or paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

Additionally, from time to time, the Company may be required to record at fair value other assets on a nonrecurring basis, such as assets held for sale and certain other assets. These nonrecurring fair value adjustments typically involve the application of lower-of-cost-or-market accounting or write-downs of individual assets.

The fair value hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets (Level 1), and the lowest priority to unobservable inputs (Level 3). The Company’s financial assets are classified within the fair value hierarchy based on the lowest level of inputs that is significant to the fair value measurement. The three levels of the fair value hierarchy, and their applicability to the Company’s financial assets, are described below.

Level 1 : Unadjusted quoted prices in active markets that are accessible at the measurement date of identical, unrestricted assets.

Level 2 : Quoted prices for similar assets, or inputs that are observable, either directly or indirectly, for substantially the full term through corroboration with observable market data. Level 2 includes investments valued at quoted prices adjusted for legal or contractual restrictions specific to the security.

Level 3 : Pricing inputs are unobservable for the assets. Level 3 assets include private investments that are supported by little or no market activity. Level 3 valuations are for instruments that are not traded in active markets or are subject to transfer restrictions and may be adjusted to reflect illiquidity and/or non-transferability, with such adjustment generally based on available market evidence. In the absence of such evidence, management's best estimate is used.

An adjustment to the pricing method used within either Level 1 or Level 2 inputs could generate a fair value measurement that effectively falls in a lower level in the hierarchy. The Company had no material re-measurements of fair value with respect to financial assets and liabilities, during the periods presented, other than those assets and liabilities that are measured at fair value on a recurring basis. Other than the warrants issued in connection with the private placement transaction which closed on September 29, 2016, the Company had no assets or liabilities classified as Level 3 as of September 30, 2018 and December 31, 2017. Transfers are calculated on values as of the transfer date. There were no transfers between Levels 1, 2 and 3 during the nine months ended September 30, 2018 and twelve months ended December 31, 2017.

The fair value of the warrants is considered a Level 3 valuation and was determined using a Monte Carlo simulation model. This model incorporated several assumptions at each valuation date including: the price of the Company's common stock on the date of valuation, the historical volatility of the price of the Company's common stock, the remaining contractual term of the warrant and estimates of the probability of a fundamental transaction occurring (See Note 6 for further discussion of the private placement).

The Company's financial instruments as of September 30, 2018 consisted primarily of cash and cash equivalents and warrant liability. The Company's financial instruments as of December 31, 2017 consisted primarily of cash, cash equivalents and marketable securities and warrant liability. As of September 30, 2018, and December 31, 2017, the Company's financial assets recognized at fair value consisted of the following:

Description	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
	(in thousands)			
September 30, 2018				
Assets:				
Cash Equivalents				
Money market funds	$3,933	$ 3,933	$ —	$ —
Total	$3,933	$ 3,933	$ —	$ —
Liabilities:				
Warrant liability	$2,155	$ —	$ —	$ 2,155
December 31, 2017				
Assets:				
Cash Equivalents				
Money market funds	$5,547	$ 5,547	$ —	$ —
Marketable securities				
Asset-backed securities	$900	$ —	$ 900	$ —

Liabilities:				
Warrant liability	$14,679	$—	$ —	$ 14,679

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs:

	September 30, 2018 (in thousands)
Beginning balance, December 31, 2017	$ 14,679
Change in fair value of warrant liability	(12,524)
Ending balance	$ 2,155

Cash and Cash Equivalents

The Company considers all highly liquid securities with original maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents are comprised of funds in money market accounts. In addition, the Company has recorded restricted cash of $0.1 million as of September 30, 2018 and December 31, 2017. Restricted cash consist of security provided for lease obligation.

Marketable Securities

The Company classifies marketable securities with a remaining maturity of greater than three months when purchased as available for sale. The Company considers all available for sale securities, including those with maturity dates beyond 12 months, as available to support current operational liquidity needs and therefore classifies all securities including those with maturity dates beyond 90 days at the date of purchase as current assets within the consolidated balance sheets. Available for sale securities are maintained by the Company's investment managers and may consist of commercial paper, high-grade corporate notes, U.S. Treasury securities, U.S. government agency securities, and certificates of deposit. Available for sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity (deficit) until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense).

If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, marks the investment to market through a charge to the Company's consolidated statement of operations and comprehensive loss.

The amortized cost of available for sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. There were no available for sale securities as of September 30, 2018.

Revenue Recognition

In May 2014, the Financial Accounting Standards Board (the "FASB") issued a new standard related to revenue recognition, Accounting Standard Update ("ASU") No. 2014-09, Revenue from Contracts with Customers. This new accounting standard will replace most current U.S. GAAP guidance on this topic and eliminate most industry-specific guidance. It provides a unified model to determine when and how revenue is recognized. The core principle is that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration for which the entity expects to be entitled in exchange for those goods or services. Entities may adopt the new standard either retrospectively to all periods presented in the financial statements (the full retrospective method) or as a cumulative-effect adjustment as of the date of adoption (modified retrospective method) in the year of adoption without applying to comparative years' financial statements. Further, in August 2015, the FASB issued ASU No. 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date, to defer the effective adoption date by one year to December 15, 2017 for annual reporting periods beginning after that date and permitted early adoption of the standard, but not before fiscal years beginning after the original effective date of December 15, 2016. The Company elected to early adopt the guidance in 2017 using the modified retrospective method. There was no cumulative impact due to the adoption of this standard.

Revenue is recognized when, or as, performance obligations are satisfied, which occurs when control of the promised products or services is transferred to customers. Revenue is measured as the amount of consideration the Company expects to receive in exchange for transferring products or services to a customer ("transaction price"). To the extent that the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing the most likely amount method. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Estimates of variable consideration and determination of whether to include estimated amounts in the transaction price are based largely on an assessment of the Company's anticipated performance and all information (historical, current and forecasted) that is reasonably available.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation based on a relative standalone selling price basis unless the

transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The Company currently generates revenue primarily through collaborative research, development and commercialization agreements. The terms of these agreements may contain multiple promises which may include: (i) licenses to the Company's technology; (ii) services related to the transfer and update of know-how; and (iii) manufacturing supply services. Payments to the Company under these arrangements typically include one or more of the following: non-refundable upfront license fees; milestone payments; royalties on future product sales; and fees for manufacturing supply services. None of the Company's contracts as of September 30, 2018 contained a significant financing component.

The Company assesses the promises to determine if they are distinct performance obligations. Once the performance obligations are determined, the transaction price is allocated based on a relative standalone selling price basis. Milestone payments and royalties are typically considered variable consideration at the outset of the contract and are recognized in the transaction price either upon occurrence or when the constraint of a probable reversal is no longer applicable.

Collaboration Revenue

While no revenue has been recognized as of September 30, 2018, the Company expects to generate revenue through collaboration and license agreements with strategic partners for the development and commercialization of product candidates. The collaboration and license agreements are within the scope of Accounting Standards Codification ("ASC 606") Revenue from Contracts with Customers.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under the agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for the arrangement, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Manufacturing Supply Services: If the promise to supply products for clinical and/or commercial development are determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from the fees allocated to the supply when or as the supply is transferred to the customer, generally upon delivery to the customer. If the promise to supply products for clinical and/or commercial development are not determined to be distinct from the other performance obligations identified in the arrangement, the Company utilizes judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue , including amounts from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes developmental and regulatory milestone payments, the Company evaluates whether the achievement of each milestone specifically relates to the Company's efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. If the achievement of a milestone is considered a direct result of the Company's efforts to satisfy a performance obligation or transfer a distinct good or service and the receipt of the payment is based upon the achievement of the milestone, the associated milestone value is allocated to that distinct good or service and revenue is recognized in the period in which the milestone is achieved. If the milestone payment is not specifically related to the Company's effort to satisfy a performance obligation or transfer a distinct good or service, the Company evaluates the milestone to determine whether the milestone is considered probable of being reached and estimates the amount to be included in the transaction price using either the most likely amount or the expected value method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price to be allocated. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall allocation. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based or usage-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of: (i) when the related sales occur; or (ii) when the performance obligation to which

some or all of the royalty has been allocated has been satisfied (or partially satisfied).

License and Collaboration Arrangements

MEDINET Co., Ltd.

In December 2017, the Company entered into a License and Commercialization Agreement (the “License Agreement”) with MEDINET Co., Ltd. (“MEDINET”) to grant MEDINET a license under certain patents, patent applications, know-how, and technology to develop and commercialize certain therapeutic products to replace or repair damaged, worn, or defective cartilage.

In exchange for the license, MEDINET agreed to pay the Company an upfront cash payment of $10.0 million which the Company received in January 2018. As of September 30, 2018, the contract with MEDINET was wholly unperformed and all revenue under the License Agreement has been deferred and has not been recognized. As of September 30, 2018, the aggregate amount of the transaction price allocated to remaining performance obligations was $10.0 million. The Company expects to recognize revenue on approximately 50% and 100% of the remaining performance obligations over the next 12 months and the following 12 months, respectively.

MEDINET also agreed to pay the Company tiered royalties, at percentages ranging from the low single digits to low double digits, of net sales of MEDINET products governed by the License Agreement. Over the life of the License Agreement, the Company is eligible to receive up to ¥330 million ($2.9 million as of September 30, 2018) in development milestone payments, $1.0 million and ¥720 million ($7.4 million as of September 30, 2018) in regulatory payments and up to an aggregate of ¥7,300 million ($64.1 million as of September 30, 2018) for the achievement of certain commercial milestones related to the sales of MEDINET products governed by the License Agreement.

As a condition of the License Agreement, the Company agreed to supply NeoCart for MEDINET's planned Phase 3 clinical trial in Japan. The Company assessed its promised goods and services under the License Agreement to determine if they are distinct. Due to the unique nature of the clinical manufacturing services to be provided by the Company, there are currently no other third-party vendors from which MEDINET can obtain such supply. The Company expects to be the only vendor capable of providing the manufacturing services for a period of at least one to two years, which is approximately the estimated length of time for the Japanese clinical trial period. After this point, if the Company were to transfer to a third-party its technology and know-how related to the manufacturing services, the third-party vendor would be capable of providing the commercial manufacturing services, and therefore MEDINET would be able to choose whether to utilize the Company for such services or another vendor. The Company determined that MEDINET's option to obtain commercial manufacturing services does not represent a material right, as the fees charged to MEDINET by the Company are expected to approximate the fair market value for manufacturing services. As noted, with the assistance of the Company, third-party vendors could have the capability to perform commercial manufacturing services by this time, and the Company expects the contract value to approximate the market price. Due to MEDINET's limitations in obtaining the clinical manufacturing services from a third-party, as well as MEDINET's limited ability to obtain the benefits of the licensed intellectual property without the clinical manufacturing services, the licensed intellectual property and clinical manufacturing services are determined to be a combined performance obligation. Based on this assessment, the Company determined that the promised goods and services do not have standalone value and are highly interrelated. Accordingly, the promised goods and services represent one performance obligation.

Based on the assessment of the combined performance obligation, the Company determined that the predominant promise in the arrangement is the transfer of the license and associated know-how expected to occur over the length of the clinical trial. The Company determined that MEDINET will be simultaneously receiving and consuming the benefits of the Company's performance related to the supply of the clinical trial. Therefore, the revenue associated with the combined performance obligation will be recognized over time.

In determining the correct measure of progress to use when recognizing revenue over time, the Company assessed whether an input or output based measure of progress would be appropriate. The Company determined that an output based measure of progress would be appropriate to use when recognizing revenue associated with the combined performance obligation. The Company will recognize revenue under the License Agreement as the clinical manufacturing services are performed. At the outset of the clinical trials to be conducted by MEDINET, the Company will have quantifiable estimates of total clinical candidates, and therefore, of total estimated performance. The Company will recognize revenue based on performance completed to date, as evidenced by the estimated number of clinical trial enrollees. The Company expects to provide the clinical manufacturing services to MEDINET over the estimated time to enroll the Japanese Phase 3 clinical trial which is currently estimated to be 12 months, beginning in the fourth quarter of 2018. Therefore, the estimated one - year clinical manufacturing period is the appropriate timing of revenue recognition for the combined performance obligation. Management will re-evaluate that estimate at each reporting period.

Revenue will be recognized using the output method over the length of the clinical trial enrollment, as the clinical manufacturing services are delivered, over the estimated one-year service period. Upon the conclusion of the clinical manufacturing period, the Company expects other third-party vendors to have the capabilities to provide similar services. At this point, the license would effectively become a distinct performance obligation, with no remaining undelivered obligations. Therefore, the Company determined that the up-front payment associated with the licensed intellectual property should be fully recognized by the conclusion of the clinical manufacturing service period.

At contract inception, the Company determined that the $10.0 million non-refundable upfront amount constituted the entirety of the consideration to be included in the transaction price as the development, regulatory, and commercial milestones represent variable consideration and were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensees' efforts. Any consideration related to sales-based

milestones (including royalties) will be recognized when the related sales occur. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company also determined that consideration associated with the clinical trials, which are payable by MEDINET on per-patient basis represent variable consideration, will be included in the transaction price upon occurrence, or once the associated clinical manufacturing service(s) for the patient are concluded.

The Company incurred cost of $0.9 million related to the License Agreement with MEDINET, of which $0.8 million was recorded as an asset that will be expensed proportionally over the performance service period.

Stock-Based Compensation

The Company accounts for stock options and restricted stock based on their grant date fair value and recognizes compensation expense on a straight-line basis over their vesting period. The Company estimates the fair value of stock options as of the date of grant using the Black-Scholes option pricing model, with the exception of stock options that include a market condition, and restricted stock based on the fair value of the underlying common stock as of the date of grant or the value of the services provided, whichever is more readily determinable. The Company, in conjunction with adoption of ASU 2016-09- Stock Compensation: Improvements to Employee Share-Based Payment Accounting has elected to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate pre-vesting option forfeitures and records stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company’s estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense is classified as research and development or general and administrative based on the grantee’s respective compensation classification.

For stock option grants with vesting triggered by the achievement of performance-based milestones, the expense is recorded over the remaining service period after the point when the achievement of the milestone is probable or the performance condition has been achieved. For stock option grants with both performance-based milestones and market conditions, expense is recorded over the derived service period after the point when the achievement of the performance-based milestone is probable or the performance condition has been achieved. For stock option grants with market conditions, the expense is calculated using the Monte Carlo model based on the grant date fair value of the option and is recorded on a straight line basis over the requisite service period, which represents the derived service period and accelerated when the market condition is satisfied. The Company did not issue awards with market conditions during the nine months ended September 30, 2018. The Company accounts for stock options and restricted stock awards to non-employees using the fair value approach. Stock options and restricted stock awards to non-employees are subject to periodic revaluation over their vesting terms.

Warrant Accounting

As noted in Note 6, Capital Stock, the Company classifies a warrant to purchase shares of its common stock as a liability on its consolidated balance sheet if the warrant is a free-standing financial instrument that may require the Company to transfer consideration upon exercise. Each warrant of this type is initially recorded at fair value on date of grant using the Monte Carlo simulation model net of issuance costs, and is subsequently re-measured to fair value at each subsequent balance sheet date. Changes in fair value of the warrant are recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. The Company will continue to adjust the liability for changes in fair value until the earlier of the exercise or expiration of the warrant.

Recent Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Changes to the Disclosure Requirements for Fair Value Measurement. The amendments in this update modify the disclosure requirements on fair value measurements based on the concepts in the Concepts Statement, including the consideration of costs and benefits. The amendments in this update are effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019 with early adoption permitted upon issuance of this Update. The Company is currently evaluating the impact that the adoption of this guidance will have on the Company’s consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share- Based Payment Accounting. This update is to simplify the aspects of accounting for nonemployee shared based payment transactions for acquiring goods or services from nonemployees. The amendments in this update are effective for fiscal years beginning after December 15, 2018, including interim periods within that year. The Company is currently evaluating the impact that the adoption of this guidance will have on the Company’s consolidated financial statements and related disclosures.

In July 2017, the FASB issued ASU No. 2017-11, Earnings Per Share (Topic 260): Distinguishing Liabilities from Equity (Topic 480); Derivatives and Hedging (Topic 815): (PART I) Accounting for certain financial instruments with down round features. This update addresses the complexity of accounting for certain financial instruments with down round features. The guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018. The Company has concluded that this guidance has no impact on the presentation of its results of operations, financial position and disclosures.

In May 2017, the FASB issued ASU No. 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting. This standard provides guidance on changes to the terms or conditions of a share based payment award that requires an entity to apply modification accounting. The guidance is effective prospectively for annual periods beginning after December 15, 2017, and for interim periods and annual periods thereafter. There were no modifications to the Company’s share based payment awards during the nine months ended September 30, 2018.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows: Restricted Cash ("ASU 2016-18"). The amendments in this update require that amounts generally described as restricted cash and restricted cash equivalents be included within cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 was effective January 1, 2018. As a result of adopting ASU 2016-18, the Company includes its restricted cash balance in the cash and cash equivalents reconciliation of operating, investing and financing activities. The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows.

	As of September 30,	
	2018	2017
	(in thousands)	
Cash and cash equivalents	$5,192	$10,798
Restricted cash	137	137
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$5,329	$10,935

In February 2016, the FASB issued ASU No. 2016-02- Leases (Topic 842). This standard requires companies to recognize on the balance sheet the assets and liabilities for the rights and obligations created by leased assets. ASU 2016-02 will be effective for the Company in the first quarter of 2019, with early adoption permitted. The Company estimates that it will recognize approximately $8 million to $10 million of right-of-use assets and corresponding lease liabilities on the balance sheet upon adoption. However, the population of contracts subject to balance sheet recognition and their initial measurement remains under evaluation; final balance sheet impacts will depend on the lease portfolio as the time of adoption. The Company does not expect that adoption will have a material impact on its results of operations or statement of cash flows.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers ("Topic 606"), which requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. In the fourth quarter of 2017, the Company early adopted ASC 606 and this standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. The Company had only one revenue arrangement as of the adoption date. Topic 606 requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. Topic 606 provides a five-step model for determining revenue recognition for arrangements that are within the scope of the standard: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for revenues, see Note 2, Revenue Recognition.

3. LOSS PER COMMON SHARE

The Company computes basic and diluted loss per share using a methodology that gives effect to the impact of outstanding participating securities (the "two-class method"). For the three and nine months ended September 30, 2018, there was dilution attributed to the weighted-average shares outstanding in the calculation of diluted loss per share.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(In thousands, except share and per share data)			
Numerator:				
Net Income (loss)	$10,785	$(5,995)	$(7,825)	$(19,618)
Net income (loss) attributable to Series A Preferred Stock (a)	135	(915)	(168)	(3,238)
Income (loss) attributable to common stockholders - basic	$10,650	$(5,080)	$(7,657)	$(16,380)
Effect of dilutive securities:				
Deduct change in fair value of warrant liability	(17,776)	—	(12,524)	—
Numerator for dilutive EPS-Earnings(loss) attributable to common stockholders after assumed conversions	$(7,126)	$(5,080)	$(20,181)	$(16,380)
Denominator:				
Weighted-average number of common shares used in earnings (loss) per	29,737,632	22,552,341	28,723,500	22,219,666

share - basic				
Effect of dilutive securities:				
Nonparticipating warrants	—	—	792,200	—
Denominator for diluted EPS-Adjusted weighted average shares	29,737,632	22,552,341	29,515,700	22,219,666
Earnings (loss) per share - basic	$ 0.36	$ (0.23)	$ (0.27)	$ (0.74)
Loss per share - diluted	$ (0.24)	$ (0.23)	$ (0.68)	$ (0.74)

(a) The Series A Preferred Stock participates in income and losses.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares outstanding, as they would be anti-dilutive (in common stock equivalent shares):

	Three and Nine months ended September 30,	
	2018	2017
Unvested restricted stock and options to purchase common stock	3,655,578	2,194,630
Series A preferred stock unconverted	177,996	3,826,920
Warrants exercisable into common stock	13,528,978	13,633,070

4. PROPERTY AND EQUIPMENT

Property and equipment consisted of the following:

	September 30, 2018	December 31, 2017
	(in thousands)	
Office equipment	$279	$ 279
Laboratory equipment	4,670	4,565
Leasehold improvements	7,711	7,712
Construction in progress	2,876	990
Software	96	96
Total property and equipment	15,632	13,642
Less: B depreciation	(11,280)	(10,919)
Property and equipment, net	$4,352	$ 2,723

Depreciation expense related to property and equipment amounted to $0.1 million and $0.4 million for the three months ended September 30, 2018 and 2017, respectively, and $0.4 million and $1.2 million for the nine months ended September 30, 2018 and 2017, respectively.

On September 5, 2018, the Company experienced a drop in stock price of 73%. As a result, the Company applied the multi-step process as described in FASB Accounting Standards Codification (“ASC”) Topic 360, “Property, Plant, and Equipment”. The first step requires the Company to determine whether there are indicators of impairment of its long-lived assets. It concluded that the drop in stock price was a triggering event for impairment. Step 2 of the process is to determine whether the carrying amount of the asset group is recoverable, based on a comparison of the total undiscounted future cash flows from the asset group to the carrying amount of the asset group. It was determined that the undiscounted cash flows are less than the carrying value of the net asset group. Step 3 is to measure the impairment loss by determining if the if the carrying value of the long-lived asset group exceeds its fair value. The Company concluded that the carrying value of the asset group did not exceed its fair value and therefore there is no impairment charge.

5. COMMITMENTS AND CONTINGENCIES

Operating Leases

The Company leases its office and research facilities in Waltham and Lexington, Massachusetts under non-cancellable operating leases. The Lexington, Massachusetts facility lease expires in June 2023. The Waltham, Massachusetts facility lease was extended in April 2017. The effective date of the extension is January 2018. Under the terms of the extension, the lease will expire in December 2024 with one extension term of five years. Terms of the agreements generally provide for an initial rent-free period and future rent escalation and provide that in addition to minimum lease rental payments, the Company is responsible for a pro-rata share of common area operating expenses.

Rent expense under operating lease agreements amounted to approximately $0.4 million and $0.2 million for the three months ended September 30, 2018 and 2017, respectively, and $1.2 million and $0.7 million for the nine months ended September 30, 2018 and 2017, respectively.

As an inducement to enter into its Lexington facility lease, the lessor agreed to provide the Company with a construction allowance of up to $1.0 million towards the total cost of tenant improvements. As an inducement to enter into the Waltham lease extension, the lessor agreed to provide the Company with a tenant improvement allowance not to exceed $0.9 million, of which $0.5 million can be applied to future rental payments. The Company has recorded these costs in the consolidated balance sheets as leasehold improvements, with the corresponding liability as deferred lease incentive. The liability is amortized on a straight-line basis over the term of the leases as a reduction of rent expense.

License Agreements

From time to time, the Company enters into various licensing agreements whereby the Company may use certain technologies in conjunction with its product research and development. Licensing agreements and the Company's commitments under the agreements are as follows:

Hydrogel License

In May 2005, the Company entered into an exclusive license agreement with Angiotech Pharmaceuticals (US), Inc. for the use of certain patents, patent applications, and knowledge related to the manufacture and use of a hydrogel material in conjunction with NeoCart and certain other products ("Hydrogel License Agreement"). As of September 30, 2018, the Company has paid an aggregate $3.2 million in commercialization milestones under the terms of the Hydrogel License Agreement, which have been expensed to research and development.

Under the terms of the Hydrogel License Agreement, the Company's future commitments include:

- A one-time $3.0 million payment upon approval of an eligible product by the FDA; and
- Single digit royalties on the net sales of NeoCart and certain other future products.

Tissue Regeneration License

In April 2001, the Company entered into an exclusive license agreement with The Board of Trustees of the Leland Stanford Junior University ("Stanford University") for the use of certain technology to develop, manufacture and sell licensed products in the field of growth and regeneration of cartilage ("Tissue Regeneration License Agreement"). The term of the Tissue Regeneration License Agreement extends to the expiration date of Stanford University's last to expire domestic or foreign patents. As of September 30, 2018, the Company has paid an aggregate $0.8 million in patent reimbursement costs, royalty fees, and commercialization milestone payments under the terms of the Tissue Regeneration License Agreement, which have been recorded to research and development expense.

Under the terms of the Tissue Regeneration License Agreement, the Company's future commitments include:

- A one-time $0.3 million payment upon approval of an eligible product by the FDA;
- An annual minimum non-refundable royalty fee of $10 thousand for the life of the license that may be used to offset up to 50% of the earned royalty below; and
- Low single digit royalties on net sales.

Honeycomb License

In March 2013, the Company entered into a license agreement with Koken Co., Ltd. ("Koken") and paid a fee for a non-exclusive, non-transferable and non-sublicensable right to use its know-how related to the process for manufacturing atelocollagen honeycomb sponge materials, which is used in scaffolds (the "Honeycomb License Agreement"). Under the terms of the Honeycomb License Agreement, future commitments will be based on the amount of materials supplied to the Company and may vary from period to period over the term of the agreement.

Tissue Processor Sub-License

In December 2005, the Company entered into an exclusive agreement to sub-license certain technology from Purpose, Co. ("Purpose"), which is owned by a stockholder of the Company ("Sub-License Agreement"). Purpose entered into the original license agreement ("Original Agreement") with Brigham and Women's Hospital, Inc. ("Brigham and Women's") in August 2001. The Original Agreement shall remain in effect for the term of the licensed patents owned by Brigham and Women's unless extended or terminated as provided for in the agreement. The technology is to be used to develop, manufacture, use and sell licensed products that cultivate cell or tissue development. The Sub-License Agreement extends to the expiration date of the last to expire domestic or foreign patents covered by the agreement. As of September 30, 2018, the Company has paid an aggregate $1.1 million in royalty and sub-license payments under the terms of the Sub-License Agreement.

The Sub-License Agreement was amended and restated in June 2012. Under the amended and restated agreement, the Company made Purpose the sole supplier of equipment the Company uses in its manufacturing processes and granted Purpose distribution rights of the Company's products for certain territories. In exchange, Purpose allowed for the use of its technology (owned or licensed) and manufactured and serviced exogenous tissue processors used by the Company. Under the terms of the agreement, as amended, Purpose granted the Company: (a) exclusive rights to all of Purpose's technology (owned or licensed) related to the exogenous tissue processors, (b) continued supply of exogenous tissue processors during the Company's clinical trials, and (c) rights to manufacture the exogenous tissue processors at any location the Company chooses. In exchange for such consideration, the Company granted Purpose an exclusive license in Japan for the use of all of the Company's technology and made a payment of $0.3 million to reimburse Purpose for development costs on a next generation tissue processor.

In May 2016, the Original Agreement was amended whereby the Company acquired the development and commercialization rights to NeoCart for the Japanese market from Purpose. Under the terms of the amended agreement, the Company assumes sole responsibility for and rights to the development and commercialization of NeoCart in Japan. In exchange for the transfer of development and commercialization rights, the Company will pay a success-based milestone to Purpose upon conditional approval of NeoCart in Japan, as well as commercial milestones and a low single digit royalty on Japanese sales of NeoCart, upon full approval, if any, in Japan.

In addition to the above, the Company's future commitments under the terms of the Original Agreement and Sub-License Agreement include:

- A minimum non-refundable annual royalty fee of $20 thousand, for the life of the license;
- An additional, non-refundable annual royalty fee of $30 thousand from 2016 through 2019;
- $10.2 million in potential milestone payments; and

- Low single digit royalties on net sales of a licensed product.

The OCS Agreement

In connection with its research and development, the Company received grants from the Office of Chief Scientist of the Ministry of Industry and Trade in Israel ("OCS") in the aggregate of $1.1 million for funding the fibroblast growth factor ("FGF") program. In consideration for this grant, the Company is committed to pay royalties at a rate of 3% to 5% of the sales of sponsored products developed using the grant money, up to the amount of the participation payments received. The Company committed to pay up to 100% of grants received plus interest according to the LIBOR interest rate if the sponsored product is produced in Israel. If the manufacturing of the sponsored product takes place outside of Israel, the royalties can increase up to, but no more than, 300% of grants received plus interest based on the LIBOR interest rate, depending on the percentage of the manufacturing of sponsored product that takes place outside of Israel.

Collagen Supply Agreement

In September 2015, the Company entered into an agreement with Collagen Solutions (UK) Limited (the "Supplier") to purchase soluble collagen that meets specifications provided by the Company. The initial term of the agreement is three years and will automatically renew from year to year thereafter unless otherwise terminated with at least 180 days' notice by either party. In February 2017, the Company entered into an amendment with the Supplier. Pursuant to the amendment, the Company agreed to pay the Supplier approximately $0.1 million in exchange for eliminating the minimum annual order of material and/or services and any other amounts due to Supplier. As of September 30, 2018, the Company has paid $0.1 million under the terms of the amendment. There is no remaining obligation to be paid.

6. CAPITAL STOCK

In March 2018, the Company entered into an equity distribution agreement ("ATM Agreement") with Canaccord Genuity Inc. ("Canaccord"), pursuant to which the Company may, from time to time, sell shares of its common stock having an aggregate offering price of up to up to $10.0 million (the "Shares") through Canaccord, as sales agent. The Shares will be offered and sold by the Company pursuant to its previously filed and currently effective Registration Statement on Form S-3 (Reg. No. 333-216741) (the "Registration Statement"). The Shares may only be offered and sold by means of a prospectus, including a prospectus supplement, forming part of the effective Registration Statement. Sales of the common stock, if any, will be made at market prices by methods deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the "Securities Act"), including sales made directly on The Nasdaq Capital Market, on any other existing trading market for the common stock, or to or through a market maker other than on an exchange. During the nine months ended September 30, 2018, the Company sold an aggregate of 5,766,247 shares of common stock and received $4.0 million after deducting commissions related to the ATM Agreement.

In January 2018, the Company completed an underwritten registered direct offering of 2,691,494 shares of common stock at a price of $2.35 per share. The total net proceeds of the offering were $5.7 million after deducting underwriter's discounts and commissions, and expenses related to the offering.

On September 29, 2016, the Company closed a private placement with certain institutional and accredited investors in which the Company received gross proceeds of $30.0 million (the "Private Placement"). The net proceeds after deducting placement agent fees and other transaction-related expenses was $27.6 million. At the closing, the Company issued 2,596,059 shares of the Company's common stock at a per share price of $2.25 and 24,158.8693 shares of the Company's newly-created Series A Convertible Preferred Stock ("Series A Preferred Stock"), which are convertible into approximately 10,737,275 shares of common stock. As of September 30, 2018, there were 400.4910 shares of Series A Preferred Stock outstanding, which remain convertible into 177,996 shares of the Company's common stock. As part of the Private Placement, the investors received warrants to purchase up to 13,333,334 shares of the Company's common stock at an exercise price of $2.25 per share. The placement agent for the Private Placement, H.C. Wainwright & Co. LLC ("HCW"), and certain of its affiliates were also granted warrants to purchase

133,333 shares of the Company's common stock with an exercise price of $2.25 per share in exchange for the services provided by HCW. The placement agent warrants were considered a financing cost of the Company and included in warrant expense within the consolidated statements of operations.

The warrants include a cashless-exercise feature that may be exercised solely in the event there is no effective registration statement, or no current prospectus available for, the resale of the shares of common stock underlying the warrants as of the six-month anniversary of the closing of the Private Placement. Upon a fundamental transaction, the holders of the warrant may require the Company to purchase any unexercised warrants in an amount equal to the Black-Scholes value of the warrant. A fundamental transaction is defined as a merger, sale of assets, sale of the Company, recapitalization of stock and a sale of stock whereby any owner after the transaction would own greater than 50% of the outstanding common stock in the Company. The warrants became exercisable following approval of the Private Placement by our stockholders in November 2016 and expire five years after the date of such stockholder approval. The Company determined the warrants are classified as a liability on the consolidated balance sheet because they contain a provision whereby in a fundamental transaction (as described above), the holder can elect to receive either the amount they are entitled to on an as-if-exercised basis or an amount based on the Black-Scholes value of the warrants at the time of the fundamental transaction. At the issuance date, the warrants were recorded at the fair value of $30.7 million and approximately $0.4 million

excess of the fair value of the liability recorded for these warrants over the proceeds received was recorded as a charge to earnings in the third quarter of 2016 and included in warrant expense within the consolidated statement of operations.

Concurrent with the closing of the Private Placement, the Company's Certificate of Incorporation was amended by the filing of a Certificate of Designation to create the Series A Preferred Stock. The Series A Preferred Stock has a par value of $0.01 and each share is convertible into 444.44 shares of common stock, at a conversion price of $2.25 per share, at the option of the holder. The Series A Preferred Stock has no voting rights and is only entitled to dividends as declared on an as-converted basis. The Series A Preferred Stock contains no liquidation preferences or redemption rights and shares in distributions of the Company on an as-converted basis with the common stock. The Series A Preferred Stock shall not be converted if, after giving effect to the conversion, the holder and its affiliated persons would own beneficially more than 4.99% of our common stock (subject to adjustment up to 9.99% solely at the holder's discretion upon 61 days' prior notice to us or, solely as to a holder, if such limitation is waived by such holder upon execution of the private placement agreement).

As part of the Private Placement, affiliates of certain members of the Company's Board of Directors purchased an aggregate of 283,046 shares of common stock, an aggregate of 2,563.1439 shares of Series A Preferred Stock and received warrants to purchase up to 1,422,221 shares of common stock at an exercise price of $2.25 per share in the Private Placement. These amounts are included in the amounts noted above.

7. WARRANTS

The Company has warrants to purchase its common stock outstanding as of September 30, 2018, as follows:

Issued	Classification	Warrants Outstanding	Exercise Price	Expiration
September 2016	Liability	13,466,667	$ 2.25	November 2021
March 2015	Equity	3,699	9.75	March 2025
July 2014	Equity	6,566	7.99	July 2024
July 2012	Equity	52,046	0.01	July 2022

8. STOCK-BASED COMPENSATION

Stock option activity under the Company's 2012 Equity Incentive Plan (the "2012 Plan") and 2013 Equity Incentive Plan (the "2013 Plan") for the nine months ended September 30, 2018 is summarized as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual	Aggregate Intrinsic Value (in thousands)

			Term (in years)	
Outstanding at December 31, 2017	2,158,348	$ 4.40	8.1	$ 436
Granted	1,530,150	2.38		
Exercised	(919)	2.56		
Cancelled	(32,001)	2.71		
Outstanding at September 30, 2018	3,655,578	$ 3.57	8.3	$ —
Vested and expected to vest at September 30, 2018	3,288,917	$ 3.69	8.2	$ —
Exercisable at September 30, 2018	1,460,898	$ 4.86	7.2	$ —

As of September 30, 2018, the unrecognized compensation cost related to outstanding options was $2.5 million and is expected to be recognized as expense over approximately 2.51 years. As of September 30, 2018, the weighted average grant date fair value of vested options was $3.25 and the weighted average grant date fair value of options outstanding was $2.33. On October 1, 2018, the Company approved a repricing of 2,774,140 stock options granted prior to September 1, 2018. See Note 12 for further discussion of the repricing.

The weighted average grant date fair value per share of employee option grants was $1.06 and $1.14 for the three months ended September 30, 2018 and 2017, respectively, and $1.77 and $1.01 for the nine months ended September 30, 2018 and 2017, respectively.

Stock-Based Compensation Expense

The Company granted stock options to employees during the three and nine months ended September 30, 2018 and 2017. The Company estimates the fair value of stock options as of the date of grant using the Black-Scholes option pricing model and restricted stock based on the stock price, with the exception of those stock options that included a market condition. The Company estimates the fair value of stock options that include a market condition using a Monte-Carlo model. Stock options and restricted stock issued to non-board member, non-employees are accounted for using the fair value approach and are subject to periodic revaluation over their vesting terms.

Stock-based compensation expense amounted to $0.4 million and $0.4 million for the three months ended September 30, 2018 and 2017, respectively, and $1.2 million and $1.2 million for the nine months ended September 30, 2018 and 2017, respectively.

The allocation of stock-based compensation for all options granted and restricted stock awards is as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(in thousands)		(in thousands)	
Research and development	$ 131	$ 86	$352	$326
General and administrative	307	283	897	907
Total stock-based compensation expense	$ 438	$ 369	$1,249	$1,233

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the employee stock option grants were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Risk-free interest rate	2.92 %	1.95 %	2.77 %	2.03 %
Expected volatility	86.4 %	60.0 %	87.5 %	63.1 %
Expected term (in years)	6.08	6.08	6.08	6.08
Expected dividend yield	0.0 %	0.0 %	0.0 %	0.0 %

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the non-employee stock option grants were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Risk-free interest rate	1.97 %	1.35 %	1.97 %	1.28 %
Expected volatility	74.0 %	59.7 %	74.0 %	63.0 %
Expected term (in years)	6.08	6.08	6.08	6.08
Expected dividend yield	0.0 %	0.0 %	0.0 %	0.0 %

9. INCOME TAXES

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets. The Company recorded no income tax expense or benefit during the nine months ended September 30, 2018 and 2017, due to a full valuation allowance recognized against its deferred tax assets.

TAX REFORM

The SEC issued Staff Accounting Bulletin No. 118 ("SAB 118") on December 22, 2017. SAB 118 provides a one-year measurement period from a registrant's reporting period that includes the Tax Cuts and Jobs Act of 2017 ("TCJA") enactment date to allow the registrant sufficient time to obtain, prepare and analyze information to complete the accounting required under ASC 740. Although the Company made a reasonable estimate of the gross amounts of the deferred tax assets as discussed in our Annual Report on Form 10-K for the year ended December 31, 2017, a final determination of the TCJA's impact on the deferred tax assets and related valuation allowance requirements remains incomplete pending a full analysis of the provisions of the TCJA and the related interpretations. The ultimate impact of the TCJA on the Company's reported results in 2018 and beyond may differ from the estimates provided therein, possibly materially, due to, among other things, changes in interpretations and assumptions the Company has made, guidance that may be issued, and other actions the Company may take as a result of the TCJA, different from what is presently contemplated. As of September 30, 2018, the Company has not recorded incremental accounting adjustments related to the TCJA as it continues to consider interpretations of its application. However, we expect to complete the accounting by December 2018.

10. EQUIPMENT LOAN PAYABLE

The Company had the following outstanding borrowing obligations for the periods indicated:

	September 30, 2018	December 31, 2017
	(in thousands)	
Silicon Valley Bank Equipment Loan Payable	$ —	$ 178
Less: current portion	—	(178)
Long-term debt, net	$ —	$ —

In July 2014, the Company entered into a loan and security agreement with Silicon Valley Bank, which provided for a line of credit to finance certain equipment purchases up to an aggregate of $1.8 million through March 31, 2015. The line was payable in 36 monthly installments of principal and interest, with an annual interest rate of 2.75% plus the greater of 3.25% and the prime rate in effect at the time of each draw, as published in the Wall Street Journal. Draws under the line of credit were secured by a first priority lien over all equipment purchased using the line of credit. The Company was in compliance with all required covenants as of December 31, 2017 and May 31, 2018 at which date the loan matured and was repaid.

In accordance with the terms of the equipment line of credit, the Company issued a warrant to Silicon Valley Bank in July 2014 to purchase 6,566 shares of its common stock at an exercise price per share of $7.99 as discussed in Note 7.

11. RELATED PARTIES

Intrexon Corporation

In September 2014, the Company entered into an Exclusive Channel Collaboration Agreement (the “Collaboration Agreement”) with Intrexon Corporation (“Intrexon”) to use Intrexon’s proprietary technology for the development and commercialization of allogeneic cell therapeutics (the “Collaboration Products”) to treat or repair damaged articular hyaline cartilage in humans. The term of the Collaboration Agreement commenced upon the effective date, September 30, 2014, and continues until either written notice of termination is given by the Company within ninety days, or if either party creates a material breach that cannot be remedied within sixty days.

Under the terms of the Collaboration Agreement, the Company is solely responsible for the costs to develop and commercialize any Collaboration Products with the following exceptions: (i) the establishment of certain manufacturing capabilities and facilities; (ii) the cost of basic research related to Intrexon’s proprietary technology outside of costs related to the Collaboration Products; (iii) payments related to certain in-licensed third party IP; (iv) the costs of filing, prosecution and maintenance of Intrexon patents; and (v) any other costs mutually agreed upon as being the responsibility of Intrexon. As partial consideration, the Company will pay commercialization milestones totaling $12 million, if and when achieved, and sales milestones totaling $22.5 million, if and when achieved. The milestone payments are payable in cash or shares of the Company’s common stock at the option of the Company. In the event the Company is sold prior to making any of these milestone payments and the Collaboration Agreement is transferred in the sale, the milestone payments would be payable in cash. The Company is also required to make low double-digit royalty payments to Intrexon on any gross profit arising from the sale of Collaboration Products and to

pay an intermediate double-digit percentage of any sublicensing revenue it receives.

Under the terms of the Collaboration Agreement, the Company reimburses Intrexon for 50% of the product research and development costs with the remaining 50% due after acceptance by the FDA or equivalent regulatory authority of an Investigational New Drug Application or equivalent regulatory filing of a collaboration product or upon 90 day written notice of cancellation by the Company. There were no expenses incurred under the collaboration for the nine months ended September 30, 2018 and 2017. The total accrued expenses due to Intrexon at September 30, 2018 and December 31, 2017 were $3.0 million and $3.0 million, respectively. These expenses were included in research and development in the consolidated statements of operations at the time they were incurred.

Purpose, Co.

In June 2012, the Company entered into an agreement with Purpose to amend its previous agreements. In the previous agreements, Purpose granted the Company a perpetual license to its patents related to its exogenous tissue processor which is used in the development of the Company's products. In exchange, the Company granted Purpose a perpetual license to all of the Company's biotechnology and biomaterial for use in Japan. The agreement provided for Purpose to manufacture and sell machinery to the Company for cost until the Company's products become commercially viable. The Company also agreed to pay royalties on any third-party revenue generated using Purpose's licensed technology.

Under the June 2012 amendment, the Company received exclusive rights to all of Purpose's technology related to the exogenous tissue processor, continued supply of exogenous tissue processors during the Company's clinical trials, and rights to manufacture the exogenous tissue processors at any location the Company chooses. In exchange for such consideration, the Company named Purpose the sole manufacturer of equipment and also clarified the geographic territories of the exclusive license that Purpose was granted for use of the Company's technology. In addition, the Company agreed to reimburse Purpose for $0.3 million of development costs on a next generation tissue processer. Refer to the discussion under Note 5, Tissue Processor Sub-License.

In May 2016, the Company acquired the development and commercialization rights to NeoCart for the Japanese market from Purpose. Under the terms of the amended agreement, the Company assumes sole responsibility for and rights to the development and commercialization of NeoCart in Japan. In exchange for the transfer of development and commercialization rights, the Company will pay a success-based milestone to Purpose upon conditional approval of NeoCart in Japan, as well as commercial milestones and a low single digit royalty on Japanese sales of NeoCart, upon full approval, if any, in Japan.

The Company paid Purpose $0.1 million and $0.1 million in the nine months ended September 30, 2018 and 2017, respectively.

12. SUBSEQUENT EVENTS

On October 10, 2018, the Company closed an underwritten public offering of 26,155,000 shares of its common stock and warrants to purchase up to 19,616,250 shares of common stock, at a combined purchase price of $0.65 per share of common stock and accompanying warrant. The gross proceeds from this offering were $17.0 million, before deducting underwriting discounts and commissions, and offering expenses payable by the Company. The warrants are exercisable immediately upon issuance at a price of $0.70 per share of common stock and have a term of five years commencing on the date of issuance.

From October 1, 2018 through November 6, 2018, the Company sold an aggregate of 867,656 shares of its common stock and received $0.5 million after deducting commissions related to the ATM Agreement.

On October 1, 2018, the Compensation Committee (the "Committee") of the Company's Board of Directors (the "Board"), following consultation with the full Board, approved a repricing of 2,774,140 stock options granted prior to September 1, 2018 (the "Repricing"). The options had exercise prices between $0.75628 and $9.97 per share, which were reduced to $0.568 per share. In connection with the Repricing, on October 1, 2018, the Committee also approved the cancelation of certain options with performance-based vesting conditions (the "Performance Options") previously issued to Messrs. Gridley, Lieber and Kennedy. Messrs. Gridley, Lieber and Kennedy were previously granted the Performance Options to purchase 60,000, 30,000 and 30,000 shares of the Company's common stock, respectively, which would vest in full if the Company's stock price was at or above $19.92 for any consecutive 60-day period within 4 years of the date of grant as long as the recipient provided continuous service during such consecutive 60-day period (the "Performance Criteria"). The Committee determined that the probability of achieving the Performance Criteria was

unlikely based on the current trading price of the Company's common stock on The Nasdaq Capital Market and cancelled the Performance Options pursuant to the Committee's authority under the 2013 Plan.

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 in conjunction with the financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q and with our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 15, 2018. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business and related financing, include forward-looking statements that involve risks, uncertainties and assumptions. You should read the "Risk Factors" and "Information Regarding Forward-Looking Statements" sections of this Quarterly Report on Form 10-Q for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leader in the development of restorative cell therapies (RCTs). We use the term RCT to refer to a new class of products we are developing that are designed to offer patients rapid-onset pain relief and restored function through the repair of damaged or worn tissue. Our lead investigational product, NeoCart, is an innovative cell therapy that utilizes various aspects of our RCT technology platform to treat tissue injury in the field of orthopedics, specifically cartilage damage in the knee. NeoCart is designed to rebuild a patient's own knee cartilage to treat pain at the source, improve function and potentially prevent a patient's progression to osteoarthritis. We have designed NeoCart to perform like articular hyaline cartilage at the time of treatment with the objective of providing patients with an accelerated recovery as compared to other alternatives, including microfracture, the current standard of care used to treat knee cartilage damage. NeoCart is one of the most rigorously studied restorative cell therapies for orthopedic use and is currently in a 249 patient, Phase 3 clinical trial. In the third quarter of 2018, we announced that our Phase 3 clinical trial of NeoCart did not meet the primary endpoint of a statistically significant improvement in pain and function in a dual threshold responder analysis one year after treatment as compared to microfracture. However, NeoCart did demonstrate statistically significant and clinically meaningful improvements on the dual threshold responder analysis six months after treatment and on nearly all individual pain and function measures when compared to microfracture one and two years after treatment. As a result, we met with the U.S. Food and Drug Administration (the FDA) on October 30, 2018 to discuss the data and a potential Biologics License Application (BLA) submission. The FDA has not made a final decision regarding a potential BLA submission. We are continuing discussions with the FDA regarding the clinical data generated to date, the potential need for any additional supplemental clinical data (which may include longer-term data from the ongoing Phase 3 clinical trial or additional studies) and potential alternative regulatory pathways for the BLA to be accepted.

In December 2017, we entered into a license agreement with MEDINET Co., Ltd. (MEDINET) for the development and commercialization of NeoCart in Japan for the replacement or repair of damaged, worn or defective cartilage. Pursuant to the terms of the license agreement, we received a non-refundable, up-front payment of $10.0 million and are eligible to receive up to an additional approximately $76.9 million in milestones, plus a transfer price for clinical and commercial supply and royalties, consisting of:

- potential regulatory and development milestone payments of up to an aggregate of approximately $10.5 million;
- sales-dependent milestones of up to an aggregate of approximately $66.4 million; and
- tiered royalties on net sales of NeoCart in Japan;

In return for such consideration, MEDINET gained exclusive commercialization rights to NeoCart in Japan. We intend to explore additional opportunities to license the rights to NeoCart in other territories outside the United States, where advanced regenerative medicine regulatory pathways may exist and appropriate market need is identified.

NeoCart is based on our RCT technology platform, which we believe has the potential to be used for a broad range of additional therapeutic indications and combines expertise in the following areas:

- Cell therapy and processing: the handling of tissue biopsies and the extraction, isolation and expansion of the cells;
- Biomaterials and Scaffold: three-dimensional biomaterials structures that enable the proper delivery, distribution and organization of cells in their natural environment to support tissue formation;
- Tissue engineering: the use of a combination of cells, engineering and biomaterials to improve or restore biological functions; and
- Bioadhesives: natural, biocompatible materials that act as adhesives for biological tissue and allow for natural cell and tissue infiltration and integration with native cells.

We have devoted substantially all of our resources to the development of our RCT platform, the preclinical and clinical advancement of our product candidates, the creation and protection of related intellectual property and the provision of general and administrative support for these operations. We have funded our operations primarily through the public and private placements of equity and debt instruments and our collaboration with MEDINET.

We have never been profitable and have incurred net losses in each year since inception. Our accumulated deficit was $216.0 million as of September 30, 2018. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect to continue to incur significant expenses and operating losses in connection with our ongoing activities as we:

- continue scale up and improvement of our manufacturing processes;
- continue with the transition of our manufacturing technology transfer;
- seek regulatory approvals and reimbursement from third-party payors and insurers for NeoCart or any other product candidates that successfully complete clinical trials;
- prepare to commercialize NeoCart, if approved;
- continue our research and development efforts;
- conduct clinical trials of any future product candidates;
- manufacture preclinical study and clinical trial materials;
- hire additional personnel to support continuing operations;
- maintain, expand and protect our intellectual property portfolio;
- implement operational, financial and management systems associated with the potential commercialization of NeoCart, if approved; and
- hire additional general and administrative personnel to operate as a public company.

We do not expect to generate any future revenue from product sales until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take place in the next few years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will seek to fund our operations through public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed, on favorable terms, or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and ability to develop our product candidates.

Financial Operations Overview

We conduct operations at our facilities in Waltham and Lexington, Massachusetts.

In May 2011, we acquired 100% of the voting shares of ProChon Biotech Ltd. (ProChon), a privately held biotechnology company focused on modulating the fibroblast growth factor system to enable it to create more effective solutions for tissue regeneration. The ProChon acquisition was accounted for as a business combination. Unless otherwise indicated, the following information is presented on a consolidated basis to include our accounts and those of ProChon subsequent to the May 2011 acquisition.

In September 2016, we completed a private placement where we issued 2,596,059 shares of the company’s common stock at a per share price of $2.25 and 24,158.8693 shares of our newly-created Series A Convertible Preferred Stock, which shares of preferred stock are convertible into approximately 10,737,275 shares of common stock. The Series A Convertible Preferred Stock will be convertible into shares of our common stock following approval of the private placement by our stockholders. The net proceeds after deduction placement agent fees and other transaction-related expenses were $27.6 million. As part of the private placement, the investors received warrants to purchase up to 13,333,334 shares of our common stock at an exercise price of $2.25 per share. The warrants include a cashless-exercise feature that may be exercised solely in the event there is no effective registration statement registering, or no current prospectus available for, the resale of the shares of common stock underlying the warrants as of the six-month anniversary of the closing of the private placement. The warrants became exercisable following approval of the private placement by our stockholders and expire five years after the date of such stockholder approval.

In January 2018, we completed an underwritten registered direct offering of 2,691,494 shares of common stock at a price of $2.35 per share. The total net proceeds of the offering were $5.7 million after deducting underwriter's discounts and commissions, and expenses related to the offering.

In March 2018, we entered into an equity distribution agreement (the Equity Distribution Agreement) with Canaccord Genuity Inc. (Canaccord), pursuant to which we may, from time to time, sell shares of our common stock (the Shares), having an aggregate offering price of up to $10 million through Canaccord, as our sales agent. The Shares will be offered and sold by us pursuant to our previously filed and currently effective Registration Statement on Form S-3 (Reg. No. 333-216741) (the Registration Statement). The Shares may only be offered and sold by means of a prospectus, including a prospectus supplement, forming part of the effective Registration Statement. Sales of the common stock, if any, will be made at market prices by methods deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the Securities Act), including sales made directly on The Nasdaq Capital Market, on any other existing trading market for the common stock, or to or through a market maker other than on an exchange. During the nine months ended September 30, 2018, we sold an aggregate of 5,766,247 shares of common stock and received $4.0 million after deducting commissions related to the Equity Distribution

Agreement and other offering costs. From October 1, 2018 through November 6, 2018, we sold an aggregate of 867,656 shares of our common stock and received $0.5 million after deducting commissions related to the Equity Distribution Agreement.

On October 10, 2018, we closed an underwritten public offering of 26,155,000 shares of our common stock and warrants to purchase up to 19,616,250 shares of common stock, at a combined purchase price of $0.65 per share of common stock and accompanying warrant. The gross proceeds from this offering were $17.0 million, before deducting underwriting discounts and commissions, and offering expenses payable by us. The warrants are exercisable immediately upon issuance at a price of $0.70 per share of common stock and have a term of five years commencing on the date of issuance.

The consolidated financial statements and following information include the accounts of Histogenics, ProChon and Histogenics Securities Corporation, a Massachusetts securities corporation. All intercompany accounts and transactions have been eliminated in consolidation.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our consolidated financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

There have been no material changes to our critical accounting policies from those described in "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 15, 2018.

Other Company Information

Net Operating Loss Carryforwards

Utilization of the net operating loss (NOL) and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred or that could occur in the future, as required by Section 382 and 383 of the Internal Revenue Code (Code), as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50% of the outstanding stock of a company by certain stockholders. We have completed a study prior to December 31, 2017, to assess whether an ownership change has occurred and the results of this study indicated we experienced ownership changes, as defined by Section 382 of the Code, in each of 2006, 2011, 2012, 2013 and 2016. We have not recorded NOLs that as a result of these restrictions will expire unused. The limitations are an aggregate of $312.8 million for the years 2010 to 2016.

As of December 31, 2017 and 2016, we had U.S. federal NOL carryforwards of $43.9 million and $24.5 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2037. As of December 31, 2017, and 2016, we also had U.S. state NOL carryforwards of $43.6 million and $24.3 million,

respectively, which may be available to offset future income tax liabilities and expire at various dates through 2037. As of December 31, 2017 and 2016, we also had $26.3 million and $26.1 million, respectively, of foreign NOL carryforwards which may be available to offset future income tax liabilities, which carryforwards do not expire.

As of September 30, 2018, we have provided a full valuation allowance for deferred tax assets.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act (JOBS Act) was enacted. Section 107 of the JOBS Act permits an “emerging growth company” or a “smaller reporting company” to delay the adoption of new or revised accounting standards until those standards would otherwise apply to private companies. We plan to avail ourselves of this exemption from new or revised accounting standards and, therefore, we may not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

For so long as we are an “emerging growth company” or “smaller reporting company,” we intend to rely on exemptions relating to: (1) providing an auditor’s attestation report on our system of internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (2) complying 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, known as the auditor discussion and analysis. We will remain an emerging growth company until the earliest of: (a) the last day of the fiscal year in which we have total

annual gross revenue of $1.0 billion or more, (b) December 31, 2019, the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering (IPO), (c) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years and (d) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Results of Operations

Three Month Periods Ended September, 2018 and 2017

The following table summarizes the results of our operations for the three month period ended September 30, 2018 and 2017:

	Three Months Ended September 30,		Change	
	2018	2017	$	%
	(in thousands)			
Research and development expenses	$4,563	$3,488	$1,075	31 %
General and administrative expenses	2,426	2,225	201	9
Other income (expense), net	17,774	(282)	18,056	(6,403)

Research and Development Expenses. Research and development expenses were $4.6 million for the three months ended September 30, 2018 as compared to $3.5 million for the three months ended September 30, 2017. The increase of $1.1 million was primarily due to increases in consulting costs of $0.9 million, and salary-related costs of $0.2 million. We expect research and development expenses to remain stable over the next three quarters due to a decline in costs related to the NeoCart Phase 3 clinical trial which we expect will be offset by an increase in costs related to a potential NeoCart BLA submission and the associated review.

General and Administrative Expenses. General and administrative expenses were $2.4 million for the three months ended September 30, 2018 as compared to $2.2 million for the three months ended September 30, 2017. The increase of $0.2 million was primarily due to increases of $0.2 million in salary-related expense and $0.2 million in consulting expenses and professional fees, which were partially offset by a decrease in depreciation of $0.2 million. We expect general and administrative expenses to rise over the next three quarters in connection with the potential commercialization of NeoCart.

Other Income (Expense), Net. Net other income (expense) was $17.8 million for the three months ended September 30, 2018 as compared to ($0.3) million for the three months ended September 30, 2017. The $18.1 million change was primarily due to a change in warrant liability caused by a decrease in our stock price in the three month period ended September 2018 relative to the three month period ended September 2017.

Nine Month Periods Ended September 30, 2018 and 2017

The following table summarizes the results of our operations for the nine month period ended September 30, 2018 and 2017:

			Change	

	Nine Months Ended September 30,			
	2018	2017	$	%
	(in thousands)			
Research and development expenses	$12,307	$12,200	$107	1 %
General and administrative expenses	8,059	6,717	1,342	20
Other income (expense), net	12,541	(701)	13,242	(1,889)

Research and Development Expenses. Research and development expenses were $12.3 million for the nine months ended September 30, 2018 as compared to $12.2 million for the nine months ended September 30, 2017. The increase of $0.1 million was primarily due to increases of $1.1 million in consulting expense, $0.8 million in materials and supplies, $0.1 million in salary-related expense, $0.2 million in repairs and maintenance and $0.1 million in sponsored research. These were partially offset by decreases of $1.7 million in clinical trial costs and $0.5 million in depreciation. We expect research and development expenses to remain stable over the next three quarters due to a decline in costs related to the NeoCart Phase 3 clinical trial which we expect will be offset by an increase in costs related to a potential NeoCart BLA submission and the associated review.

General and Administrative Expenses. General and administrative expenses were $8.1 million for the nine months ended September 30, 2018 as compared to $6.7 million for the nine months ended September 30, 2017. The increase of $1.4 million was primarily due to an increase of $0.8 million in salary-related expense, $0.5 million in consulting expenses and professional fees and $0.4 million in facility-related costs which were partially offset by a $0.3 million decrease in depreciation. We expect general and administrative expenses to rise over the next three quarters in connection with the potential commercialization of NeoCart.

Other Income (Expense), Net. Net other income (expense) was $12.5 million for the nine months ended September 30, 2018 as compared to ($0.7) million for the nine months ended September 30, 2017. The $13.2 million change was primarily due to a change in warrant liability caused by a decrease in our stock price in the nine month period ended September 2018 relative to the nine month period ended September 2017.

Liquidity and Capital Resources

We have incurred losses and negative cash flows from operations resulting in an accumulated deficit at September 30, 2018 of $216.0 million. We anticipate that we will continue to incur net losses for the next several years. Through September 30, 2018, we have funded our consolidated operations primarily through funds from the sale of equity securities, commercial bank debt, payments from collaboration activities, and, to a limited extent, revenue from product sales and grants. As of September 30, 2018, we had cash and cash equivalents $5.2 million.

We believe that our existing cash and cash equivalents will be sufficient to fund our projected cash needs into the middle of 2019. However, we will require additional capital to sustain operations through FDA approval of NeoCart, if at all, and to commercialize NeoCart, if approved. To meet our capital needs, we intend to raise additional capital through debt or equity financings, or other strategic transactions. However, there can be no assurances that we will be able to complete any such transaction on acceptable terms or otherwise. The failure to obtain sufficient funds on commercially acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition. Accordingly, these factors, among others, raise substantial doubt about our ability to continue as a going concern.

The following table sets forth a summary of the net cash flow activity for each of the periods indicated:

	Nine Months Ended September 30,		Change	
	2018	2017	$	%
	(in thousands)			
Net cash used in operating activities	$(8,839)	$(18,701)	$9,862	(53)%
Net cash used in investing activities	(1,040)	(1,977)	937	(47)
Net cash provided by (used in) financing activities	7,990	(432)	8,422	(1,950)
Net increase (decrease) in cash and cash equivalents	$(1,889)	$(21,110)	$19,221	(91)%

Operating Activities

Cash used in operating activities decreased $9.9 million to $8.8 million for the nine months ended September 30, 2018 from $18.7 million for the nine months ended September 30, 2017. During the nine months ended September 30, 2018, net cash used in operating activities was driven primarily by our net loss of $7.8 million, $12.5 million related to a change in the fair value of warrant liability and a $0.9 million net change in operating assets and liabilities which were partially offset by deferred revenue of $10.0 million from our license agreement with MEDINET, $1.2 million from stock-based compensation, a $0.8 million charge for deferred rent and lease incentive and $0.4 million of depreciation expense..

Investing Activities

Cash used in investing activities decreased $0.9 million to $1.0 million for the nine months ended September 30, 2018 from $2.0 million for the nine months ended September 30, 2017. The decrease was primarily due to purchases of fixed assets of $1.9 million in 2018 compared to $0.1 million in 2017 and $0.9 million of net proceeds from the maturities of marketable securities in 2018 compared to $1.8 million of net purchases of marketable securities in 2017.

Financing Activities

Cash provided by financing activities increased $8.4 million for the nine months ended September 30, 2018 primarily due to net proceeds received from the sale of common stock of $8.2 million after deducting the underwriter's discounts and commissions, and expenses related to the offerings.

Operating Capital Requirements

We anticipate that we will continue to incur losses for the next several years in connection with the continuing development of NeoCart. In addition, we expect the losses to increase as we seek regulatory approvals for NeoCart and any future product candidates and begin to commercialize any approved products. We are subject to all risks inherent in the development of new therapeutic products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in the future in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from sales of our products, if ever, we expect to finance future cash needs through public or private equity or debt offerings. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Any of these events could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. The amount and timing of future funding requirements, both near- and long-term, will depend on many factors, including:

- the outcome, timing and cost of regulatory approvals by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than, or evaluate clinical endpoints other than those that we currently expect;
- the timing and costs associated with our manufacturing technology transfer;
- the timing and costs associated with manufacturing NeoCart and our future product candidates for clinical trials, preclinical studies and, if approved, for commercial sale;
- the cost of establishing sales, marketing and distribution capabilities for NeoCart, or any products for which we may receive regulatory approval;
- our ability to obtain adequate reimbursement from payors for any product which may be commercialized, if approved;
- the design, initiation, progress, size, timing, costs and results of non-clinical studies and clinical trials for our product candidates;
- the number and characteristics of product candidates that we pursue;
- the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need to expand our research and development activities, including our need and ability to hire additional employees;
- our need to implement additional infrastructure and internal systems and hire additional employees to operate as a public company and prepare to support the commercialization of NeoCart, if approved; and
- the effect of competing technological and market developments.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Off-Balance Sheet Arrangements

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

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

Not applicable.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act), are controls and other procedures designed to ensure that information required to be disclosed in reports filed or submitted under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified by the rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to management, including the chief executive officer and the chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

In connection with the preparation of this Quarterly Report on Form 10-Q, we completed an evaluation, as of September 30, 2018, under the supervision of and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, as to the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). It should be noted that any system of controls, however well designed and operated, can provide only reasonable, and not absolute, assurance that the objectives of the system will be met. In addition, the design of any control system is based in part upon certain assumptions about the likelihood of future events.

During the third quarter of 2018, the Company identified a material weakness in the Company's internal controls relating to the valuation of the warrant liability. Because the valuation of the warrants is exceedingly complex and requires highly specialized skills to perform and review, the Company uses the assistance of a third-party service provider to perform such valuation. In the third quarter of 2018, the third-party service provider made an error in the valuation that was not detected by management in its review process but was identified by the Company's

independent registered public accounting firm prior to the issuance of the Company's financial statements for the period covered by the valuation analysis

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or detected on a timely basis. The identified material weakness did not result in a misstatement to the Company's consolidated financial statements or disclosures; however, it could result in misstatements of certain account balances (such as warrant liability and change in fair value of warrant liability) or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. The Company plans to implement additional review procedures, including engaging a second third-party service provider to assist in its review of the work of the third-party service provider preparing the valuation analysis

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we are subject to claims in legal proceedings arising in the normal course of its business. We do not believe that we are currently party to any pending legal actions that could reasonably be expected to have a material adverse effect on our business, financial condition, results of operations or cash flows.

Item 1A. Risk Factors.

The following description of risk factors include any material changes to, and supersedes the description of, risk factors associated with our business previously disclosed in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the Securities and Exchange Commission (SEC) on March 15, 2018, under the heading "Risk Factors." Our business, financial condition and operating results can be affected by a number of factors, whether currently known or unknown, including but not limited to those described below, any one or more of which could, directly or indirectly, cause our actual operating results and financial condition to vary materially from past, or anticipated future, operating results and financial condition. Any of these factors, in whole or in part, could materially and adversely affect our business, financial condition, operating results and the price of our common stock.

The following discussion of risk factors contains forward-looking statements. These risk factors may be important to understanding any statement in this Quarterly Report on Form 10-Q or elsewhere. The following information should be read in conjunction with the consolidated financial statements and related notes in Part I, Item 1, "Financial Statements" and Part I, Item 2, "Management's, Discussion and Analysis of Financial Condition and Results of Operations."

Because of the following factors, as well as other factors affecting our financial condition and operating results, past financial performance should not be considered to be a reliable indicator of future performance, and investors should not use historical trends to anticipate results or trends in future periods.

Risks Related to Our Business and Commercialization of Our Product Candidates

The United States Food and Drug Administration (the FDA) may not accept a Biologics License Application (BLA) submission for NeoCart and, even if the FDA accepts and files our BLA, the FDA may not approve NeoCart.

We met with the FDA on October 30, 2018 to discuss the results of our Phase 3 clinical trial of NeoCart announced in the third quarter of 2018 and the potential BLA submission. There can be no assurance that the FDA will accept a BLA submission for filing for NeoCart, in particular in light of the results of our Phase 3 clinical trial, in which NeoCart did not meet its primary endpoint. In the event that the FDA determines that the data from our Phase 3 clinical trial or other required information are not sufficiently complete to permit a substantive review of a BLA, we would need to evaluate our ability to generate additional data or conduct additional trials that might permit a BLA submission. There can be no assurance that we would be able to generate any additional data, conduct any additional trials or that the additional data would support a submission of the BLA, and, as a result, we may be unable to seek FDA approval for NeoCart. Further, even if the FDA accepts our BLA for NeoCart, the results of our Phase 3 clinical trial may decrease the likelihood that the FDA approves NeoCart. If we are unable to seek FDA approval for NeoCart or if the FDA denies approval for NeoCart, we will be unable to commercialize NeoCart. If we are not able to commercialize NeoCart, or are significantly delayed in doing so, our business will be materially harmed and we may need to curtail or cease operations.

We are a clinical-stage cell therapy company with a limited operating history of developing late-stage product candidates. There is a limited amount of information about us upon which to evaluate our product candidates and business prospects, making an investment in our common stock unsuitable for many investors.

We are a clinical-stage company focused on the development of restorative cell therapies (RCTs). We use the term RCT to refer to a new class of products we are developing that are designed to offer patients rapid-onset pain relief and restored function through the repair of damaged or worn tissue. We were formed in 2000 and have a limited operating history. Since inception we have devoted substantially all of our resources to the development of our cell therapy technology platform, the clinical and preclinical advancement of our product candidates, the creation, licensing and protection of related intellectual property rights and the provision of general and administrative support for these operations. We have not yet obtained regulatory approval for any product candidates in any jurisdiction or generated any significant revenues from product sales. If NeoCart or any of our future product candidates fails in clinical trials or preclinical development, or does not gain regulatory approval, or if our product candidates following regulatory approval, if any, do not achieve market acceptance, we may never become profitable or sustain profitability.

We commenced our first clinical trial in 2005, and we have a limited operating history developing clinical-stage RCTs upon which you can evaluate our business and prospects. In addition, besides our current ongoing NeoCart Phase 3 clinical trial, we have never conducted clinical trials of a size required for regulatory approvals. Further, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, such as cell therapy. For example, to execute our current business plan we will need to successfully:

- complete and submit a BLA for NeoCart following our meeting with the FDA on October 30, 2018;

- execute our research and development strategies, for NeoCart or any future products we may develop;
- complete the transition of the NeoCart raw material manufacturing processes to our in-house facilities and satisfy the FDA as to the comparability of such raw materials to those manufactured by third parties to support the BLA for NeoCart or any additional filings related to changes to the BLA that we may make after the commercialization of NeoCart, if approved;
- secure additional funding as may be needed, including, without limitation, to complete the NeoCart Phase 3 clinical trial, and commercialize NeoCart, if approved;
- obtain required regulatory approvals for the manufacturing and commercialization of NeoCart;
- obtain adequate reimbursement from third-party payors for NeoCart or any other product that may be commercialized, if approved;
- manage our spending as costs and expenses increase due to BLA preparation, potential regulatory approvals, manufacturing and potential commercialization and increased operational requirements (which may include, for example the banking of cell biopsies);
- continue to build and maintain a strong intellectual property portfolio;
- recruit and retain qualified executive management and other personnel;
- build and maintain appropriate research and development, clinical, sales, manufacturing, financial reporting, distribution and marketing capabilities on our own or through third parties;
- expand potential indications of NeoCart and our RCT technology platform;
- gain broad market acceptance for our product candidates; and
- develop and maintain successful strategic relationships.

If we are unsuccessful in accomplishing any of these objectives, we may not be able to develop product candidates, raise capital, expand our business or continue our operations.

Failure to obtain, or any delay in obtaining, FDA approval regarding the comparability of critical NeoCart raw materials following our technology transfer and manufacturing location transition may have an adverse effect on our business, operating results and prospects.

We are in the process of transitioning the manufacturing of certain raw materials and components in the NeoCart supply chain from outsourced contract manufacturers to in-house manufacturing facilities. This technology transfer currently extends to our source collagen and collagen honeycomb scaffold. In the future, we also intend to transition the three primary components of the CT3 bioadhesive – methylated collagen, curing component and activated polyethylene glycol – from outsourced contract manufacturers to in-house manufacturing facilities.

We have also entered into a supply agreement with Collagen Solutions (UK) Limited (Collagen Solutions) pursuant to which we may request the manufacture of additional collagen used in our manufacture of NeoCart. We currently do not anticipate using any collagen produced by Collagen Solutions in the near future. However, we may need additional supplies of collagen or other critical raw materials above those we anticipate being able to produce in-house after commercialization, if ever.

Although we do not anticipate changes to the raw materials, formulations or properties, nor do we anticipate material changes to the NeoCart manufacturing process or finished product specifications as a result of the transfers we are in the process of making or may make in the future, we are required to demonstrate to the FDA that the raw materials manufactured in our facility, and which may be manufactured under our direction in third-party facilities (including, without limitation, facilities operated by Collagen Solutions or other third-party manufacturers) are comparable to the raw materials that were manufactured in the previous contract manufacturers' facilities. Demonstrating comparability requires evidence that the product is consistent with that produced for the clinical trial to assure that the technology transfer does not affect safety, identity, purity or efficacy during the expansion from pilot scale to full scale production. For example, in April 2016, the FDA approved our submission which provided equivalence data for the collagen manufactured at our Lexington, Massachusetts facility which would indicate that the collagen manufactured at such facility will require no further additional data or actual patient equivalence studies. Similarly, in August 2016, the FDA notified us that it approved our collagen scaffold equivalence strategy to use biomechanical data, once

available, which we previously submitted in May 2016. However, there can be no assurance we will not be required to provide additional data to the FDA to support the approval of the NeoCart BLA.

In the future, the FDA may determine that such analytical data is not sufficient to prove comparability of the raw materials produced at our in-house manufacturing sites, or the sites of third parties under our direction, to the raw materials sourced from external vendors for earlier clinical trial work, including the NeoCart Phase 3 clinical trial. If this is the case, the FDA may require that we provide additional comparability preclinical or clinical data to provide evidence to support the comparability of the raw materials. The size, scope, length and costs of any new or supplemental testing or clinical trials that may be required by the FDA to provide such data are not known at this time. Failure or delay in obtaining FDA approval of the comparability of our NeoCart raw materials or the FDA requiring us to provide additional clinical data may result in delays to our current projected timelines and could have an adverse effect on our business, operating results and prospects.

Additionally, our manufacturing sites, or those of third-party sites under our direction, may not receive FDA approval to operate at all, resulting in delays while we implement improvements necessary to receive approval which would lead to delays in the initiation of commercial production. In

addition, we could encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel, leading to additional delays. Specifically, after the approval of NeoCart, if any, by the FDA we will only have one manufacturing suite in operation. In the event we encounter problems with that suite, we could be prohibited from supplying NeoCart to support commercialization activities or any future clinical trials. Failure to rapidly address and correct any such problems could have an adverse effect on our business, operating results and prospects.

We are heavily dependent on the success of our lead product candidate NeoCart, which is still under development in a Phase 3 clinical trial. If we are unable to obtain FDA approval for NeoCart, commercialize NeoCart in the future, or experience significant delays due to manufacturing or otherwise in doing so, our business will be materially harmed.

We have invested a significant portion of our time and financial resources in the development of NeoCart, our product candidate in clinical development. We anticipate that in the near term our ability to generate revenues will depend solely on the successful development, FDA approval, if at all, and commercialization of NeoCart. We may not complete our registration filings in our anticipated time frame. Even after we complete our BLA submission, the FDA may not accept our submission, may request additional information from us, including data from additional preclinical or clinical trials, and, ultimately, may not grant marketing approval for NeoCart. In addition, the clinical data we have generated to date is susceptible to varying interpretations and many companies that have believed that their products performed satisfactorily in clinical trials have nonetheless failed to obtain FDA approval for their products.

If we are not successful in commercializing NeoCart, or are significantly delayed in doing so, our business will be materially harmed and we may need to curtail or cease operations. Our ability to successfully commercialize NeoCart will depend, among other things, on our ability to:

- complete and submit the BLA for NeoCart;
- produce, through a validated process, NeoCart in quantities sufficiently large to permit successful commercialization;
- receive marketing approvals from the FDA and similar foreign regulatory authorities;
- obtain adequate reimbursement from third-party payors for NeoCart, if approved;
- build a commercial infrastructure and launch commercial sales of NeoCart, including the training of physicians in the use of NeoCart;
- successfully monitor patients during and after treatment and minimize the risk that enrolled subjects will drop out of the NeoCart Phase 3 clinical trial before they are evaluated for additional endpoint data for future evaluation;
- maintain adequate capital resources to fund operations through commercialization; and
- secure acceptance of NeoCart in the medical community and with third-party payors.

We have incurred significant losses since our inception and anticipate that we will continue to incur substantial losses for the next several years.

We have incurred net losses in each year since our inception, including net losses of $26.4 million in 2017 and $16.2 million in 2016. As of September 30, 2018 and December 31, 2017, we had an accumulated deficit of $216.0 million and $208.2 million, respectively. We expect to continue to incur substantial losses for the next several years, and we expect these losses to increase as we continue our development of and seek regulatory approval for, NeoCart and potentially develop future product candidates. In addition, if we receive regulatory approval to market NeoCart or any of our future product candidates, we will incur additional losses as we scale our manufacturing operations and build an internal sales and marketing organization to commercialize any approved products. In addition, we expect our expenditures to increase as we add infrastructure and personnel to support our expanding operations in connection with the commercialization of NeoCart, if approved. We anticipate that our net losses and accumulated deficit for the next several years will be significant as we conduct our planned operations. Given our current development plans, we anticipate that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations into the middle of 2019. Accordingly, these factors, among others, raise substantial doubt about our ability to continue as a going concern. Because of the numerous risks and uncertainties associated with the development and commercialization of cell therapies, we are unable to accurately predict the timing or amount of the development and

clinical expenses or when, or if we will be able to achieve, or maintain, profitability. In addition, our expenses could increase if we are required by the FDA or comparable foreign regulatory authorities to perform preclinical or clinical studies or trials in addition to those currently expected, or if there are any delays in our current or future efforts to complete the technology transfer and manufacturing location transition of our NeoCart raw material manufacturing process or completing our clinical trials or the development and commercialization of NeoCart or our future product candidates. The amount of our future net losses will depend, in part, on the amount and timing of our expenses, our ability to generate revenue and our ability to raise additional capital. These net losses have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not available, may require us to delay, reduce or cease our product development activities and operations.

We are currently advancing our lead product candidate NeoCart through clinical development and BLA submission to the FDA. Developing cell therapies and combination products, such as NeoCart, including conducting preclinical studies and clinical trials, is expensive. We will require substantial additional capital in order to file a BLA for NeoCart with the FDA, create additional manufacturing capacity for and to commercialize NeoCart and conduct the research and development and clinical and regulatory activities necessary to bring other product candidates to market. If

the FDA or comparable foreign regulatory authorities require that we perform additional manufacturing comparability testing, preclinical studies or clinical trials at any point or expand or extend our current trials, our expenses would further increase beyond what we currently expect, and the anticipated timing of any future clinical development activities and potential regulatory approvals may be delayed depending upon our allocation of resources and available funding. Raising funds currently or in the then-current economic environment may be difficult and additional funding may not be available on acceptable terms, or at all.

The global economic volatility and market instability has made the business climate more volatile and more costly. These economic conditions, and uncertainty as to the general direction of the macroeconomic environment, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, or on acceptable terms, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of manufacturing, sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

The amount and timing of our funding requirements will depend on many factors, including:

- the timing of and costs involved in obtaining NeoCart regulatory approvals, including the submission of the BLA for NeoCart;
- the scope, progress, expansion, costs and results of our clinical trials;
- the scope, timing and costs of manufacturing NeoCart implants;
- the timing of and costs associated with obtaining FDA approval of the comparability of the NeoCart and NeoCart raw materials manufactured in our facilities, or in third-party facilities at our direction, with the raw materials that were manufactured by third-parties for the use in our NeoCart clinical trials;
- market acceptance of NeoCart following the receipt of regulatory approval, if any;
- our ability to obtain adequate reimbursement from third-party payors for NeoCart or any other product that may be commercialized, if approved;
- the resources we devote to marketing and commercializing NeoCart, if approved;
- the scope, progress, expansion and costs of the commercial manufacturing of NeoCart;
- our ability to raise capital through the issuance of additional shares of our common stock or convertible securities is restricted by the limited number of our residual authorized shares and the potential difficulty of obtaining stockholder approval to increase authorized shares;
- the costs of maintaining, expanding and protecting our intellectual property portfolio, including potential litigation costs and liabilities associated therewith; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems, and quality and pharmacovigilance systems related to our status as a public company and the potential commercialization of NeoCart, if approved.

Many of these factors are outside of our control. Based upon our currently expected level of operating expenditures, we believe that we will be able to fund our operations into the middle of 2019. Our expectations are based on management's current assumptions, regulatory submission timelines and clinical development plans, which may prove to be wrong, and we could spend our available financial resources much faster than we currently expect. This period could be shortened if there are any unanticipated increases in spending on development programs or other unanticipated increases in spending related to circumstances outside of our control, including, without limitation, costs associated with litigation or other legal proceedings, hiring of additional consultants and personnel or procurement of additional raw materials. Our existing cash and cash equivalents will not be sufficient to obtain regulatory approval. Accordingly, we continue to require substantial additional capital. In order to fund our future capital needs, we may seek additional funding through equity or debt financings, development partnering arrangements, lines of credit or other sources.

Our fundraising efforts in the future to secure additional financing will divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to significantly delay, reduce or discontinue the development or commercialization of one or more of our product candidates or curtail our operations, which will have an adverse effect on our business, operating results and prospects.

NeoCart and our future product candidates are subject to extensive regulation, compliance with which is costly and time consuming, may cause unanticipated delays or prevent the receipt of the approvals required to commercialize NeoCart and our future product candidates.

The clinical development, manufacturing, quality assurance, labeling, storage, record-keeping, advertising, promotion, pharmacovigilance, import, export, marketing and distribution of NeoCart and our future product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years, and can vary

substantially based upon the type, complexity, and novelty of the products involved, as well as the target indications. Approval policies or regulations may change and the FDA has substantial discretion in the approval process for cell therapies and combination products, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the our interpretation of the data from our NeoCart Phase 3 clinical trial, the design or implementation of our NeoCart Phase 3 clinical trial or any of our future development partners' clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from the United States;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials or the use of results from studies that served as precursors to our current or future product candidates;
- such authorities may find deficiencies in our manufacturing processes or facilities or those of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- biologic, device or combination product approval policies, classifications and corresponding regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the risks described above, can involve additional product testing, administrative review periods, and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals or biologics may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new cell therapy products based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

If NeoCart or any future product candidate that we successfully develop does not achieve broad market acceptance among physicians, patients, third-party payors and the medical community, the revenue that it generates and the success of our operations may be limited.

Even if NeoCart or our future product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, third-party payors and the medical community. Coverage and timely reimbursement of our product candidates by third-party payors, including government payors, generally is also necessary for commercial success. The degree of market acceptance of any approved product candidates will depend on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the clinical indications and label claims for which our product candidate is approved;
- acceptance by physicians, major operators of hospitals and clinics and patients of our product candidate as a safe and effective treatment;
- the number of alternative treatments on the market and the potential and perceived advantages of our product candidates over such alternative treatments;

- the safety of product candidates seen in a broader patient group, including their use outside the approved indications;
- the cost of treatment relative to alternative treatments;
- the availability of timely adequate reimbursement and pricing by third parties and government authorities;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse events;
- the effectiveness of our sales and marketing efforts; and
- unfavorable publicity or regulations relating to our product candidates, competitive products, either on the market or in development, or cell or tissue therapies, in general.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, third-party payors and patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Ethical, social and legal concerns about cell or tissue therapies could result in additional regulations restricting or prohibiting the use of our product candidates.

Additionally, if any of our competitors' products are approved and are unable to gain market acceptance for any reason, there could be a market perception that products like NeoCart are not able to adequately meet an unmet medical need. If we are unable to demonstrate to physicians, hospitals, third-party payors and patients that our products are better alternatives, we may not be able to gain market acceptance for our products at the levels we anticipate and our business may be materially harmed as a result.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The process of manufacturing NeoCart is complex, highly regulated and subject to several risks, including:

- The process of manufacturing NeoCart, including the use of autologous cells, is susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or surgeon or laboratory technician error. Even minor deviations from normal manufacturing processes could result in lost NeoCart production runs, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing process or facilities in which our products are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which NeoCart is made could be adversely affected by equipment failures, labor shortages, natural disasters, power failures and numerous other factors. For instance, in 2012, we voluntarily suspended manufacturing operations and paused enrollment of the NeoCart Phase 3 clinical trial upon discovery of discrepancies in the testing procedures used to assess one of the raw materials utilized in the manufacture of NeoCart implants and we could be required in the future to suspend manufacturing due to circumstances out of our control.
- We and our third-party contract manufacturers must comply with the current Good Manufacturing Practices (cGMP) regulations and guidelines promulgated by the FDA. We and our third-party contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and third-party our contract manufacturers are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption or other issues that arise in the manufacture, packaging, storage or shipping of our products as a result of a failure of our facilities or operations, or the facilities or operations of third parties, to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products. These potential failures may lead to significant delays in the availability of products for our clinical studies or the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our products or may be subject to product recalls, seizures, injunctions, or criminal prosecution.
- Any adverse developments affecting manufacturing operations for our products may result in shipment delays, clinical enrollment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.

In order to manufacture NeoCart, we operate our own cGMP manufacturing facility in Waltham, Massachusetts for production of NeoCart. In 2015, we completed the buildout of a facility for our cGMP manufacturing in Lexington,

Massachusetts which we plan to further qualify to produce key NeoCart raw materials, including certain of the CT3 components, source collagen and collagen scaffold. In 2018, we made renovations to our cGMP manufacturing facility in Waltham, Massachusetts for production of the initial commercial supply of NeoCart upon FDA approval, if granted. While we own the manufacturing process, unforeseen issues or outside influences could impact potential supply. For example:

- Our facility in Waltham may not meet FDA cGMP standards during the pre-approval inspection necessary for BLA approval, or our recent renovations may not be viewed as sufficiently comparable by the FDA during the BLA review, delaying BLA approval and resulting in added cost to mitigate issues identified during inspection.
- Our Lexington, Massachusetts facility for production of key raw materials may not receive FDA approval to operate, resulting in delays while we implement improvements necessary to receive approval, leading to delays in the initiation of commercial production of NeoCart. We met with the FDA in December 2014 to obtain preliminary feedback and general acceptance of our raw material transition strategy. In April 2016, the FDA approved our production of collagen and the use of collagen in the NeoCart Phase 3 clinical trial. In addition, in August 2016, the FDA also approved our collagen scaffold equivalence strategy subject to the submission of data that demonstrates the comparability of the scaffold used in the prior NeoCart clinical trials to scaffolds we produce. Additionally, we have entered into a supply agreement with Collagen Solutions pursuant to which we may request the manufacture of additional collagen used in our manufacture of NeoCart. Any raw materials manufactured or handled at facilities

operated by Collagen Solutions or other third-party manufacturers will similarly need to be approved by the FDA for comparability, and the FDA may delay approval of the new raw material source or require additional studies to show comparability. We are not currently using any collagen produced by Collagen Solutions. However, we may need additional supplies of collagen above those we anticipate being able to produce in-house after commercialization, if ever.

- The raw material to be produced at our facilities may not be comparable to the raw materials sourced from external vendors for earlier clinical trial work, including the ongoing NeoCart Phase 3 clinical trial, according to our current projected timelines, and the FDA may delay approval of the new raw material source or require additional studies to show comparability. Such delays may impact the timing of our BLA submission for NeoCart and FDA approval, if granted at all.
- We may not achieve our anticipated production throughput targets, resulting in lower than anticipated capacity, limiting supply of our products, lowering revenue and increasing costs. We may not hit our production cost target for a variety of reasons including increased raw material cost, underestimate of labor requirements, underestimate of capital requirement and other facility, personnel or materials issues that we have not anticipated. Increased costs will adversely impact gross margin achieved by our products.
- We may not be able to fund on a timely basis future expansions of additional clean rooms and associated equipment and validations to support NeoCart production and to meet market demand, or the FDA may require additional data that may delay our ability to supply anticipated market needs.
- The FDA may not approve implementation of a multi-unit or improved NeoCart reactor or other production improvements or such approvals may be delayed, which could result in capacity limitation and higher unit costs.

NeoCart or any future product candidate we or any of our future development partners advance into clinical trials may cause unacceptable adverse events or have other properties that may delay or prevent its regulatory approval or limit its commercial potential.

Unacceptable adverse events caused by NeoCart or any of our future product candidates that we advance into clinical trials could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This in turn could prevent us from completing development or commercializing the affected product candidate and generating revenue from its sale.

We have not yet completed clinical testing of any of our product candidates for the treatment of the indications for which we intend to seek approval, and we currently do not know the extent of adverse events, if any, that will be observed in individuals who receive any of our product candidates. If any of our product candidates cause unacceptable adverse events in clinical trials, we may not be able to obtain regulatory approval or commercialize such product candidates.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval.

The development of cell therapies and combination products has inherent risk. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. The development of a cell therapy is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement and completion of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of biologics under development result in the submission of a BLA to the

FDA and even fewer are approved for commercialization.

Development of cell therapies is inherently expensive and risky and may not be understood by or accepted in the marketplace, which could adversely affect our future value.

The clinical development, commercialization and marketing of cell therapies are at an early-stage, substantially research-oriented, and financially speculative. To date, very few companies have been successful in their efforts to develop and commercialize cell therapies. In general, cell therapies may be susceptible to various risks, including undesirable and unintended side effects, unintended immune system responses, inadequate therapeutic efficacy, potentially prohibitive costs or other characteristics that may prevent or limit their approval or commercial use. Furthermore, the number of people who may use cell- or tissue-based therapies is difficult to forecast with accuracy. Our future success is dependent on the establishment of a large global market for cell therapies and our ability to capture a share of this market with NeoCart and our future product candidates.

Our development efforts with our cell therapy technology platform are susceptible to the same risks of failure inherent in the development and commercialization of product candidates based on new technologies. The novel nature of cell therapies creates significant challenges in the areas of product development and optimization, manufacturing, government regulation, third-party reimbursement and market acceptance.

Even if we successfully develop and obtain regulatory approval for NeoCart and our future product candidates, the market may not understand or accept them. NeoCart and our future product candidates represent novel treatments and are expected to compete with a number of surgical options and more conventional products and therapies manufactured and marketed by others, including major pharmaceutical and biotechnology companies. The degree of market acceptance of any of our developed and potential product candidates will depend on a number of factors, including:

- the clinical safety and effectiveness of NeoCart and our future product candidates and their perceived advantage over alternative treatment methods, if any;
- the design of the trial protocol for our NeoCart Phase 3 clinical trial and the data generated in the trial;
- adverse events involving NeoCart and our future product candidates or the products or product candidates of others;
- the performance and price of NeoCart and the competitive products in the market; and
- the cost of manufacturing our products, the selling price of our products, and the reimbursement policies of government and private third-party payors.

If the healthcare community does not accept NeoCart or our future product candidates for any of the foregoing reasons, or for any other reason, it could affect our sales, having an adverse effect on our business, financial condition and results of operations.

We have a limited manufacturing capacity for NeoCart and our future product candidates, which could inhibit our revenues and the long-term growth prospects of our business.

We currently produce materials for clinical trials, including production of NeoCart, at our existing manufacturing facilities in Waltham, Massachusetts, which we have designed and operated to be compliant with FDA and other regulatory authorities', cGMP and the current Good Tissue Practice as and if applicable, requirements. While we believe these facilities provide us with sufficient capacity to meet our expected clinical demand and our initial commercial launch demand, it is possible that the demand for products could exceed our existing manufacturing capacity. It will become necessary or desirable for us to expand our manufacturing capabilities for our cell therapy technology platform in the future, which may require us to invest significant amounts of capital and to obtain additional regulatory approvals. We may not be able to fund future expansions of additional clean rooms and associated equipment and validations to support NeoCart production, or the FDA or other regulatory authorities may require additional data that may delay our ability to supply anticipated market needs. If we are unable to meet rising demand for products on a timely basis or unable to maintain cGMP compliance standards, then it is likely that our clients and potential clients will elect to pursue alternative treatment options, which could materially and adversely affect the level of our revenues and our prospects for growth.

Our expected initial capacity to manufacture NeoCart implants at launch, if approved, is limited by both space and equipment. For example, the current tissue engineering processor (TEP) in our Waltham facility is resource dependent due to its single-unit capacity. We are developing plans to innovate and automate our manufacturing equipment and processes with a goal of providing adequate and timely capacity to meet expected demand after the initial launch. The FDA may not, however, approve of the equipment modifications and automation plans or approval may be delayed which could result in capacity limitation or high unit costs depending upon the length of the delay.

Components of cell therapies, such as medical devices and other constituents, that are approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP requirements. In addition, the manufacturing process for cell therapies and combination products may be required to be modified from time to time in response to FDA or other regulatory authorities' requests. Manufacture of cell- or tissue-based therapies is complex

and subjects companies to significant regulatory burdens that may change over time. We may encounter difficulties in the production of our product candidates due to our limited manufacturing experience or due to the fact that we will only have one manufacturing suite in operation through the initial phase of commercialization, if any.

Insurance coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Market acceptance and sales of NeoCart and our future product candidates will depend significantly on the availability of adequate timely insurance coverage and reimbursement from third-party payors for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medical treatments they will pay for and establish reimbursement levels. 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 candidate 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.

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our product candidates to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that timely coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that the reimbursement process and reimbursement amounts will not reduce the demand for, or the price of, NeoCart or our future product candidates. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved. In the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to health care systems that could affect our ability to sell our product candidates profitably. This has resulted in lower rates of reimbursement. There have been numerous other federal and state initiatives designed to reduce payment for products.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new cell or tissue therapies. They may also refuse to provide coverage of approved product candidates for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved cell or tissue therapies, which in turn will put pressure on the pricing of such products. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative proposals as well as country, regional, or local healthcare budget limitations.

In addition, reimbursement agencies in foreign jurisdictions may be more conservative than those in the United States. Accordingly, in markets outside the United States, the reimbursement for our products may be more limited than in the United States and may be insufficient to generate commercially reasonable revenues and profits.

Failure to obtain or maintain adequate reimbursement for any products for which we receive marketing approval will adversely impact our ability to achieve commercial success.

We may pursue additional indications and conduct additional clinical trials for NeoCart or other products we may develop in the future. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We are required to identify and enroll a sufficient number of patients that meet inclusion criteria under investigation for our clinical trials, including, for example, a future NeoCart clinical trial in pediatric patients with knee cartilage damage. There is a limited patient population from which to draw participants in clinical trials. We may not be able to identify and enroll a sufficient number of patients, or those with required or desired characteristics and criteria, in a timely manner. In addition, there are a limited number of specialized orthopedic surgeons that perform cartilage repair implantation procedures and among physicians who perform such procedures, some may not choose to perform these procedures under conditions that fall within our protocols, which would have an adverse effect on our development of product candidates. For example, in November 2015 we changed our guidance for the completion of patient enrollment in the NeoCart Phase 3 clinical trial from June 2016 to June 2017 based on enrollment trends in November 2015 not meeting our expectations. We completed enrollment in the NeoCart Phase 3 clinical trial in June 2017.

Our ability to enroll patients in any future clinical trials is affected by a number of factors including:

- the size and nature of the patient population;
- the design of and adherence to the trial protocol for our clinical trials;
- the eligibility and exclusion criteria for the trial in question;

- the availability of competing therapies and competing clinical trials, and physician and patient perception of our product candidates and our other product candidates being studied in relation to these other potential options;
- the efforts to facilitate timely enrollment in clinical trials;
- the ability to obtain and maintain patient consent;
- the number and location of clinical sites in our clinical trials;
- the proximity and availability of clinical trial sites for prospective patients;
- the availability of time and resources at the institutions where clinical trials are and will be conducted;
- the availability of raw materials and the possibility of raw materials expiring prior to their use;
- the availability of adequate financing to fund ongoing clinical trial expenses;
- the presence of concomitant joint disease in patients under investigation; and

- the study endpoints such as pain that rely on subjective patient reported outcomes.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have an adverse effect on our business.

A number of cell and tissue therapy companies have suffered significant setbacks or difficulty enrolling patients in later stage clinical trials even after achieving promising results in earlier stages of development. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and initial results from a clinical trial do not necessarily predict final results. Even if early stage clinical trials are successful, we may need to conduct additional clinical trials for product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell these product candidates. Our failure to demonstrate the required characteristics to support marketing approval for NeoCart and our product candidates in our current and future clinical trials would substantially harm our business and prospects.

If our competitors develop treatments for the target indications of NeoCart or our future product candidates that are approved more quickly, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

The cell and tissue therapy sector is intensely competitive and subject to rapid and significant technological change. We face competition from major multinational companies, established and early-stage biotechnology companies, and universities and other research institutions. Many of our competitors have greater financial and other resources, such as larger research and development staff and more experienced marketing and manufacturing organizations. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing products. These companies also have significantly greater research, sales and marketing capabilities and collaborative arrangements in our target markets with leading companies and research institutions. Established 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. As a result of all of these factors, our competitors may succeed in obtaining patent protection or FDA approval or discovering, developing and commercializing treatments in the indications that we are targeting before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

There are several clinical-stage development programs in various stages of development that seek to regenerate soft tissue and repair cartilage. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, technologies and products that are more effective, including a one-step alternative to NeoCart, or less costly than NeoCart or any future product candidates that we may develop, which could render our products obsolete and noncompetitive.

We believe that our ability to successfully compete will depend on, among other things:

- our ability to fund our operations at levels that enable us to appropriately manage the risks associated with the development, regulatory process and potential commercialization of NeoCart and any other product candidates we may develop in the future;
- the results of our and our collaborative partners' preclinical studies and clinical trials;
    - the relative prices and perceived value of competitive products as compared to NeoCart;
- our ability to recruit and enroll patients for our clinical trials;
- the relative efficacy, safety, ease of use, reliability and durability of our product candidates, including the ease of logistics and reliability of delivery of our product to our customers;
- the speed at which we and our competitors develop our respective product candidates, and any improvements to those candidates;

- our ability to design and successfully execute appropriate clinical trials;
- our ability to commercialize and market any of our product candidates that receive regulatory approval;
- our ability to manufacture raw materials and NeoCart implants for use in any future clinical trials or commercial supply, if approved;
- our ability to manufacture and sell commercial quantities of any approved products to the market;
- our ability to protect and develop intellectual property rights related to our products;
- the timing and scope of regulatory approvals, if any;
    - our ability to maintain a good relationship with regulatory authorities;
- market perception and acceptance of cell or tissue therapies;
- acceptance of our product candidates by physicians, patients and institutions;
- the cost to manufacture and price of our products; and
    - adequate levels of reimbursement under private and governmental health insurance plans, including Medicare.

If our competitors market products that are more effective, safer or less expensive than our future products or that reach the market sooner than our future products, we may not achieve commercial success. In addition, market reception to MACI, another product offered to treat knee cartilage defects could negatively impact a future launch of NeoCart following FDA approval, if at all. Any inability to compete effectively will adversely impact our business and financial prospects.

Our current and potential future commercialization, license or collaboration agreements for NeoCart or any other product candidate may place some or all aspects of the development and commercialization of NeoCart or other product candidates in countries other than the United States outside our control, and may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

We have entered into and may in the future enter into additional license or collaboration agreements with third parties for the development or commercialization of NeoCart or future product candidates. In December 2017, we entered into a License and Commercialization Agreement with MEDINET Co., Ltd. (MEDINET) with regards to the commercialization of NeoCart in Japan (the MEDINET Agreement). Our likely collaborators for any commercialization, distribution, marketing, licensing or other collaboration arrangements in jurisdictions outside the United States include pharmaceutical and biotechnology companies such as MEDINET. Because such collaborators are independent third parties, they may be subject to different risks than we are and may have significant discretion in, and different criteria for, determining the efforts and resources they will apply related to their agreements with us. We may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend in part on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates are subject to numerous risks, which may include the following:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to any such collaborations. For instance, the MEDINET Agreement, provides that they are responsible for conducting the Japanese Phase 3 clinical trial of NeoCart, and for regulatory and commercialization activities in Japan.
- Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical study results, changes in their strategic focus, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities.
- Collaborators may assume responsibility for conduct of clinical trials for product candidates in certain geographies and may fail to conduct such trials, may conduct them improperly, or may generate data inconsistent with the data from our clinical trials.
- Collaborators may assume responsibility for seeking or maintaining regulatory approvals, pricing, government reimbursement approval and public and private formulary placements. Failure to effectively obtain such approvals and clearances will substantially impact the commercial potential for the product candidate. For example, following completion of the Phase 3 clinical trial of NeoCart in Japan, MEDINET will be responsible for Japanese regulatory activities, including submitting the application for Japanese Marketing Authorization to the PMDA to obtain initial marketing approval.
- Collaborators may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study, abandon a product candidate, repeat or conduct new clinical studies or require a new formulation of a product candidate for clinical testing.
- Collaborators may be required to conduct duplicate analytical testing of a product candidate or approved product upon importation to a specific jurisdiction. If, for example, MEDINET conducts limited release testing of NeoCart for sale in Japan, data generated could be inconsistent with the testing conducted by us or other third parties upon initial release, which would require investigation and resolution and could impact our ability to continue distribution of released material.
- Collaborators could acquire or independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates.

- A collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution. For example, MEDINET is responsible for all sales, marketing and related activities for NeoCart in Japan and if it fails to adequately resource these functions, the product is unlikely to reach expected revenue targets for Japan.

- The actions of a collaborator may create liability for us as the global manufacturer of a product candidate, either directly or through indemnification obligations defined in license, collaboration or other agreements.
- Collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability.
- Collaborators may publish or otherwise publicly present or disclose information regarding our product candidates, including laboratory data or the results of preclinical or clinical research.
- Disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our product candidates or that results in costly litigation or arbitration that diverts management attention and resources.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

- Collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

If we are not successful in discovering, developing, acquiring and commercializing additional product candidates, our ability to expand our business will be limited.

A substantial amount of our effort is focused on the continued clinical testing and potential approval of NeoCart and our future product candidates and expanding our product candidates to serve other indications of high unmet medical needs. Research programs to identify other indications require substantial technical, financial and human resources, whether or not any product candidates for other indications are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If we do not successfully develop and commercialize product candidates for other indications, our business and future prospects may be limited and our business will be more vulnerable to problems that we encounter in developing and commercializing our current product candidates.

We may fail to comply with any of our obligations under existing agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that are material to our business.

We are a party to technology licenses that are important to our business and we may enter into additional licenses in the future. We currently hold material licenses from Purpose Co., Ltd., Angiotech Pharmaceuticals (US), Inc., Angiodevice International GmbH, the Board of Trustees of The Leland Stanford Junior University, Koken Co., Ltd., Intrexon and Advanced BioMatrix, Inc. The rights licensed under these agreements, including rights relating to our scaffolds, tissue processor, bioadhesives and growth factors, are material to our cell therapy technology platform and the continued development of NeoCart and our future product candidates. These licenses impose various commercial, contingent payment, royalty, insurance, indemnification and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we would lose valuable rights under our license agreements and our ability to develop or commercialize product candidates. Any termination or reversion of our rights to under the foregoing agreements may have a material adverse effect on our business, prospects and results of operations. Our Exclusive Channel Collaboration Agreement (the ECC) with Intrexon Corporation (Intrexon) provides that Intrexon may terminate such agreement if we do not perform certain specified requirements, including developing therapies considered demonstrably superior to existing therapies and those under development by us.

We may experience delays in commencing or conducting our clinical trials or in receiving data from third parties or in the completion of clinical testing, which could result in increased costs to us and delay our ability to generate product candidate revenue.

Before we can initiate clinical trials in the United States for our product candidates, we need to submit the results of preclinical testing to the FDA as part of an IND, along with other information including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol. We may rely in part on preclinical, clinical and quality data generated by contract research organization and other third parties for regulatory

submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND, which may lead to additional delays and increase the costs of our preclinical development. Despite the presence of an active IND for a product candidate, clinical trials can be delayed for a variety of reasons including delays in:

- identifying, recruiting and training suitable clinical investigators;
- reaching agreement on acceptable terms with prospective contract research organizations and trial sites, the terms of which can be subject to extensive negotiation, may be subject to modification from time to time, and may vary significantly among different contract research organizations and trial sites;
- manufacturing and obtaining sufficient quantities of a product candidate for use in clinical trials, including as a result of transferring the manufacturing of a product candidate to another site or manufacturer or the procurement of critical raw materials required for manufacturing a product candidate;

- obtaining and maintaining institutional review board or ethics committee approval to conduct a clinical trial at an existing or prospective site;
- identifying, recruiting and enrolling subjects to participate in a clinical trial; and
- retaining or replacing participants who have initiated a clinical trial but may withdraw due to adverse events from the therapy, insufficient efficacy, fatigue with the clinical trial process, or personal issues.

The FDA may also put a clinical trial on clinical hold at any time during product candidate development. In addition, we may voluntarily pause a clinical trial for a variety of reasons. For instance, in 2012 we voluntarily suspended manufacturing operations and paused enrollment of the NeoCart Phase 3 clinical trial upon discovery of discrepancies in the testing procedures used to assess one of the raw materials utilized in the manufacture of NeoCart implants and we could be required in the future to suspend manufacturing due to circumstances out of our control.

Once a clinical trial has begun, it may also be delayed as a result of ambiguous or negative interim results. Further, a clinical trial may be suspended or terminated by us, an institutional review board, an ethics committee or a data safety monitoring committee overseeing the clinical trial, any of our clinical trial sites with respect to that site or the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities;
- unforeseen safety issues, known safety issues that occur at a greater frequency or severity than we anticipate, or any determination that the clinical trial presents unacceptable health risks; or
- lack of adequate funding to continue the clinical trial.

Any delays in the commencement of our clinical trials will delay our ability to pursue regulatory approval for our product candidates. Changes in U.S. and foreign regulatory requirements and guidance to cell therapies or combination products also may occur and we may need to conduct additional preclinical studies or amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to institutional review boards for re-examination, which may affect the costs, timing and likelihood of a successful completion of a clinical trial. If we or any of our future development partners experience delays in the completion of, or if we or any of our future development partners must terminate, any clinical trial of any product candidate our ability to obtain regulatory approval for that product candidate will be delayed and the commercial prospects, if any, for the product candidate may suffer as a result. In addition, many of these factors may also ultimately lead to the denial of regulatory approval of a product candidate.

Regulatory authorities, including the FDA, PMDA and the European Medicines Agency, may disagree with our interpretations of data from pre-clinical studies and clinical trials, or change requirements related to these studies and trials. Regulatory authorities also may approve a product for narrower indications than requested or may grant approval subject to the performance of post-marketing studies for a product. There can be no guarantee that such post-approval studies, if required, will corroborate the results of earlier trials. Furthermore, the market use of such products may show different safety and efficacy profiles to those demonstrated in the trials on which marketing approval was based. Such circumstances could lead to the withdrawal or suspension of marketing approval for the product, which could have a material adverse effect on our business, financial condition, operating results or cash flows. In addition, regulatory authorities may not approve or agree with the labeling claims that are necessary or desirable for the successful commercialization of our products.

We may face product liability claims 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 NeoCart and our future product candidates in clinical trials 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 participants in clinical trials, consumers, healthcare providers, pharmaceutical companies or others

selling or otherwise coming into contact with our product candidates and any products for which we obtain marketing approval. There is a risk that our product candidates may induce adverse events, and that such adverse events may not be detected for a long period of time. 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:

- impairment of our business reputation;
- withdrawal of clinical trial participants;

- termination of clinical trial sites or entire trial programs;
- increased costs due to related litigation;
- 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 product liability insurance that we believe 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 cell or tissue therapies or medical treatments that had unanticipated adverse effects. In addition, under some of our agreements with clinical trial sites, we are required to indemnify the sites and their personnel against product liability and other claims. A successful product liability claim or series of claims brought against us or any third parties whom we are required to indemnify could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

During the course of treatment, patients may suffer adverse events 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 development and commercialization efforts, delay our regulatory approval process, 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.

We do not carry insurance for all categories of risk that our business may encounter and we may not be able to receive or maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

If we are unable to establish sales and marketing capabilities or fail to enter into agreements with third parties to market and sell any product candidates we may successfully develop, we may not be able to effectively market and sell any such product candidates.

We have no experience selling and marketing any products. We do not currently have any infrastructure or personnel for the sale, marketing and distribution of any of our product candidates upon approval, if at all, and we must build this infrastructure in order to commercialize any product candidates for which we may obtain approval in the United States or make arrangements with third parties to perform these functions for us outside of the United States. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. The establishment and development of a sales force, either by us or jointly with a development partner, or the establishment of a contract sales force to market any product candidates we may develop will be expensive and time consuming and could delay any commercial launch. If we or any of our future development partners are unable to establish sales and marketing capabilities or any other nontechnical capabilities necessary to commercialize any product candidates we may successfully develop, we will need to contract with third parties to market and sell such product candidates. We may not be able to establish arrangements with third parties on acceptable terms, if at all.

The technologies on which our channel partnering agreement with Intrexon is based are currently in the preclinical stage of development. The intellectual property of Intrexon underlying the ECC may be subject to infringement or other challenges, similar to those we face, as set forth elsewhere in these risk factors.

Our ECC with Intrexon that provides for the worldwide exclusive use of Intrexon's proprietary synthetic biology technology platform for the development and commercialization of allogeneic genetically modified chondrocyte cell therapeutics for the treatment or repair of damaged articular hyaline cartilage in humans. Such technologies have a limited history of use in the design and development of human therapeutic product candidates and may therefore involve unanticipated risks or delays. We cannot assure that any product candidates developed from this collaboration will result in nonclinical results sufficient to warrant the advancement of such product candidates into human clinical trials.

To the extent the intellectual property protection of any of the assets owned or licensed, or needed to be owned or licensed by Intrexon utilized under our ECC with Intrexon are successfully challenged or encounter problems, including, without limitation, restrictions on freedom to operate, with the United States Patent and Trademark Office or other comparable agencies throughout the world, the future development or commercialization, if any, of these potential products could be delayed or prevented. Any challenge to the intellectual property protection of intellectual property owned or licensed by Intrexon of a potential development asset arising from our ECC with Intrexon could harm our business have an adverse effect on our financial condition and results of operations.

Significant developments arising from the current political climate in the United States and U.K. could have a material adverse effect on us.

The current presidential administration has expressed antipathy towards existing trade agreements such as the North American Free Trade Agreement, greater restrictions on free trade generally and significant increases on tariffs on goods imported into the United States, particularly from China and Mexico. Changes in United States social, political, regulatory and economic conditions or in laws and policies governing foreign trade, manufacturing, development and investment, and any negative sentiments towards the United States as a result of such changes, could adversely affect our business.

Additionally, on June 23, 2016, the United Kingdom held a referendum and voted in favor of leaving the European Union. On February 1, 2017, the United Kingdom parliament voted to allow the United Kingdom to exit the European Union by passing a bill that gives the prime minister of the United Kingdom the authority to invoke Article 50 of the Lisbon Treaty. This referendum has created political and economic uncertainty, particularly in the United Kingdom and the European Union, and this uncertainty may last for years. There are many ways in which our business could be affected, only some of which we can identify.

The referendum, and the likely withdrawal of the United Kingdom from the European Union, it triggers, has caused and, along with events that could occur in the future as a consequence of the United Kingdom's withdrawal, including the possible breakup of the United Kingdom, may continue to cause significant volatility in global financial markets, including in global currency and debt markets. This volatility could cause a slowdown in economic activity in the United Kingdom, Europe or globally, which could adversely affect our operating results and growth prospects. In addition, our business could be negatively affected by new trade agreements between the United Kingdom and other countries, including the United States, and by the possible imposition of trade or other regulatory barriers in the United Kingdom, especially if the United Kingdom withdraws from the European Union. These possible negative impacts, and others resulting from the United Kingdom's actual or threatened withdrawal from the European Union, may adversely affect our operating results and growth prospects as well as the manner in which we conduct our business operations in Europe.

Changes in government funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, properly administer drug innovation, or prevent new products and services from being developed or commercialized by our life science tenants, 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 budget and funding levels, ability to hire and retain key personnel, 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 government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

In December 2016, the 21st Century Cures Act was signed into law. This new legislation is designed to advance medical innovation and empower the FDA with the authority to directly hire positions related to drug and device development and review. In the past, the FDA was often unable to offer key leadership candidates (including scientists) competitive compensation packages as compared to those offered by private industry. The 21st Century Cures Act is designed to streamline the agency's hiring process and enable the FDA to compete for leadership talent by expanding the narrow ranges that are provided in the existing compensation structures.

In the first week of the new presidential administration, it issued executive orders to freeze government hiring of new employees with the exception of military, national security and public safety personnel. This hiring freeze could impede current or future operations at the FDA and other agencies. It is unknown at this time what the impact of the hiring freeze will have on the FDA and on programs such as the 21st Century Cures Act. Furthermore, future government proposals to reduce or eliminate budgetary deficits may include reduced allocations to the FDA and other

related government agencies. These budgetary pressures may result in a reduced ability by the FDA to perform their respective roles; including the related impact to academic institutions and research laboratories whose funding is fully or partially dependent on both the level and timing of funding from government sources.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs, biologics and devices to be reviewed and/or approved by necessary government agencies and the healthcare and drug industries' ability to deliver new products to the market in a timely manner, which would adversely affect our tenants' operating results and business. Interruptions to the function of the FDA and other government agencies could adversely affect the demand for office/laboratory space and significantly impact our operating results and 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 furlough critical FDA employees. If a prolonged government shutdown occurs, it could delay the acceptance, review and any approval of the NeoCart BLA.

Legislative or regulatory healthcare reforms in the United States and abroad may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, market and distribute our products after approval is obtained.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory approval, manufacture and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of NeoCart or any future product candidates. Recent presidential and congressional elections in the U.S. could result in significant changes in, and uncertainty with respect to, legislation, regulation and government policy that could significantly impact our business and the health care industry. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- additional studies, including clinical studies;
- recall, replacement, or discontinuance of one or more of our products;
- the payment of additional taxes; or
- additional record keeping.

Each of these requirements would likely entail substantial time and cost and could adversely harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory approvals for any future products would harm our business, financial condition and results of operations. We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to such product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

We currently rely on third parties in order to perform certain aspects of our business, including to support certain aspects of our clinical trials and to supply certain raw materials and the NeoCart tissue engineering processor. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties to monitor our investigative clinical sites and monitor and manage data for our ongoing clinical programs. For example, we rely on these parties for the collection and reporting of our primary and secondary endpoint data, execution of our clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We also rely on third parties to assist in conducting our nonclinical studies in accordance with good laboratory practices. We and our third-party service providers are required to comply with good clinical practices, which are regulations and guidelines enforced by the FDA, as well as comparable foreign regulations and guidelines, for all of our product candidates in clinical development. Regulatory authorities enforce these good clinical practices through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party service providers or clinical trial sites fail to comply with applicable good clinical practices, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with good clinical practices requirements. In addition, our clinical trials must be conducted with product produced under applicable good manufacturing practices requirements. Failure to comply with these regulations may require us to repeat nonclinical and clinical trials, which

would delay the regulatory approval process.

Our third-party service providers are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going clinical and nonclinical programs. If third-party service providers do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party service providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Although we carefully manage our relationships with our third-party service

providers, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We are also dependent on third-party suppliers, most of which are sole source suppliers of certain raw materials used in the manufacture of NeoCart, and of the components used to manufacture our TEP. If these third-party suppliers do not supply sufficient quantities to us on a timely basis and in accordance with applicable specifications and other regulatory requirements, there could be a significant interruption of our ability to supply, which would adversely affect clinical development or commercial production of the product candidate. Furthermore, if any of these third parties cannot successfully supply TEPs that we require for our production that conforms to our specifications and with regulatory requirements, we will not be able to meet demand, for our product candidates.

We do not expect to have the resources or capacity to commercially manufacture TEPs required to manufacture our proposed product candidates if approved, and will likely continue to be dependent on third-party suppliers. Our dependence on third parties to manufacture and supply us with these TEPs may adversely affect our ability to develop and commercialize our product candidates on a timely basis.

We have also entered into a supply agreement with Collagen Solutions pursuant to which we may oversee the manufacture of additional collagen used in our manufacture of NeoCart. We currently do not anticipate using any collagen produced by Collagen Solutions during our Phase 3 clinical trial or to support our commercialization activities in the U.S. However, we may need additional supplies of collagen above those we anticipate being able to produce in-house upon commercialization, if ever.

We may not be successful in establishing and maintaining development or other strategic partnerships, which could adversely affect our ability to develop and commercialize product candidates.

As part of our strategy, we intend to enter into development or other strategic partnerships in the future, including collaborations with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate partners and the negotiation process is time consuming and complex. Moreover, we may not be successful in our efforts to establish a development or commercialization partnership or other alternative arrangements for any of our other existing or future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early a stage of development for collaborative effort or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market.

Moreover, if we fail to establish and maintain development or other strategic partnerships related to our product candidates:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

We will need to expand our operations and increase the size of our company and we may experience difficulties in managing any such growth.

As we continue to advance NeoCart towards potential commercialization, increase the number of ongoing product development programs and advance our future product candidates through preclinical studies and clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities and, in some cases, collaborate and contract with third parties to provide these capabilities for us. Our management, personnel and information and quality systems currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees or consultants with the requisite expertise and experience;
- manage our preclinical and clinical programs effectively;
    - develop a marketing and sales infrastructure if we receive regulatory approval for any product candidate;
- continue to improve our operational, financial and management controls, reporting systems and procedures, including those related to being a public company that is potentially manufacturing and selling commercial products; and
- construct, validate and effectively operate new and expanded manufacturing facilities, along with the required logistical, quality systems, information systems and distribution capabilities that may be required upon approval.

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

If we fail to attract and keep senior management and key scientific personnel, the future development and commercialization of our product candidates may suffer, harming future regulatory approvals, sales of our product candidates or our results of operations.

We are highly dependent on members of our management and scientific teams, including Adam Gridley, our Chief Executive Officer and President; Donald Haut, Ph.D., our Chief Business Officer; E. Lynne Kelley, M.D., our Chief Medical Officer; Stephen Kennedy, our Chief Operating Officer; and Jonathan Lieber, our Chief Financial Officer. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We do not maintain “key person” insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, particularly in the greater Boston area. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.

Given the specialized nature of cell and tissue therapy and that it is a relatively new field, there is an inherent scarcity of experienced personnel in the field. We may not be able to attract or retain qualified management, finance, sales and marketing, scientific and clinical personnel and consultants due to the intense competition for qualified personnel and consultants among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced high turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of our senior management team. The loss of Mr. Gridley or one or more additional executive officers or key employees, could seriously harm our ability to implement our business strategy successfully. While we have entered into employment contracts 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. Replacing key personnel and consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel and consultants. Our failure to retain key personnel or consultants could materially harm our business, and the transition to any replacement personnel, particularly at the chief executive officer position, may cause or result in:

- speculation and uncertainty about our business and future direction;
- distraction of our employees and management;
- difficulty in recruiting, hiring, motivating and retaining talented and skilled personnel;
- volatility in our stock price; and
- difficulty in negotiating, maintaining or consummating business or strategic relationships or transactions.

We rely on our scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist them in developing products or technologies that may compete with ours. If we are unable to maintain consulting relationships with our key advisors or consultants or if they provide services to our competitors, our development and commercialization efforts will be impaired, and our business will be significantly harmed.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal control requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act and the related rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Pursuant to Section 404 of the Sarbanes-Oxley Act and related rules, our management will be required to report upon the effectiveness of our internal control over financial reporting when we are no longer a "smaller reporting company" or an "emerging growth company," each as defined under the Exchange Act. When and if we are a "large accelerated filer" or an "accelerated filer" and are no longer an "emerging growth company," each as defined in the Exchange Act, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 for a period of no more than five years. Once we are no longer an emerging growth company or smaller reporting company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we need to: upgrade our systems, including information technology; implement additional financial and management controls, reporting systems and procedures; and hire additional accounting and finance staff. The timing of implementation of these changes may coincide with the potential commercialization of NeoCart, which may divert the time and resources of the management and other employees during commercialization activities in order to comply with the enhanced requirements.

We are also subject to complex tax laws, regulations, accounting principles and interpretations thereof. The preparation of our financial statements requires us to interpret accounting principles and guidance and make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our interpretations, estimates and judgments are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for the preparation of our financial statements. U.S. generally accepted accounting principles presentation is subject to interpretation by the SEC, the Financial Accounting Standards Board and various other bodies formed to interpret and create appropriate accounting principles and guidance. In the event that one of these bodies disagrees with our accounting recognition, measurement or disclosure or any of our accounting interpretations, estimates or assumptions, it may have a significant effect on our reported results and may retroactively affect previously reported results. The need to restate our financial results could, among other potential adverse effects, result in us incurring substantial costs, affect our ability to timely file our periodic reports until such restatement is completed, divert the attention of our management and employees from managing our business, result in material changes to our historical and future financial results, result in investors losing confidence in our operating results, subject us to securities class action litigation, and cause our stock price to decline.

We have identified material weaknesses in our internal controls over financial reporting and may identify additional material weaknesses in the future that may cause us to fail to meet our reporting obligations or result in material misstatements of our financial statements.

Our management team is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with U.S. generally accepted accounting principles. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis.

During the third quarter of 2018, we identified a material weakness in our internal controls relating to the valuation of the warrant liability. Because the valuation of the warrants is exceedingly complex and requires highly specialized skills to perform and review, we use the assistance of a third-party service provider to perform such valuation. In the

third quarter of 2018, the third-party service provider made an error in the valuation that was not detected by us in our review process but was identified by our independent registered public accounting firm prior to the issuance of our financial statements for the period covered by the valuation analysis. The identified material weakness did not result in a misstatement to our consolidated financial statements or disclosures; however, it could result in misstatements of certain account balances (such as warrant liability and change in fair value of warrant liability) or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. We plan to implement additional review procedures, including engaging a second third-party service provider to assist in our review of the work of the third-party service provider preparing the valuation analysis.

We cannot assure you that we will not have additional material weaknesses or significant deficiencies in our internal control over financial reporting. If we identify any other material weaknesses or significant deficiencies that may exist, 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, and our stock price may decline materially as a result.

If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.

From time to time we have considered, and we will continue to consider in the future, strategic business initiatives intended to further the expansion and development of our business. These initiatives may include acquiring businesses, technologies or products or entering into a business combination with another company.

For instance, in 2011, we acquired ProChon Biotech Ltd. Although we intend to evaluate and consider acquisitions, reorganizations and business combinations in the future, we have no agreements or understandings with respect to any acquisition, reorganization or business combination at this time. Any acquisitions we undertake, including our prior acquisition of ProChon Biotech Ltd., will likely be accompanied by business risks which may include:

- the effect of the acquisition on our financial and strategic position and reputation;
- the need to reprioritize our development programs and even cease development and commercialization of our product candidates;
- the failure of an acquisition to result in expected benefits, which may include benefits relating to enhanced revenues, technology, human resources, costs savings, operating efficiencies, goodwill and other synergies;
- the difficulty, cost and management effort required to integrate the acquired businesses, including costs and delays in implementing common systems and procedures and costs and delays caused by communication difficulties;
- the assumption of certain known or unknown liabilities of the acquired business, including litigation-related liabilities;
- the reduction of our cash available for operations and other uses, the increase in amortization expense related to identifiable assets acquired, potentially dilutive issuances of equity securities or the incurrence of debt;
- a lack of experience in new markets, new business culture, products or technologies or an initial dependence on unfamiliar distribution partners;
- the possibility that we will pay more than the value we derive from the acquisition;
- the impairment of relationships with customers, partners or suppliers of the acquired business; and
- the potential loss of key employees of the acquired company.

These factors could harm our business, results of operations or financial condition.

In addition to the risks commonly encountered in the acquisition of a business or assets as described above, we may also experience risks relating to the challenges and costs of evaluating or closing a transaction, including distraction of our management team from normal business operations. The risks described above may be exacerbated as a result of managing multiple acquisitions at once.

U.S. federal income tax reform could adversely affect us.

On December 22, 2017, U.S. federal tax legislation, commonly referred to as the Tax Cuts and Jobs Act (TCJA), was signed into law, significantly reforming the U.S. Internal Revenue Code (the Code). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest, allows for the expensing of capital expenditures, puts into effect the migration from a “worldwide” system of taxation to a territorial system and modifies or repeals certain business deductions and credits.

We continue to examine the impact the TCJA may have on our business. We will evaluate the effect of the TCJA on our net operating losses and our projection of taxes. As a result of the passage of the TCJA, corporate tax rates in the United States will decrease in 2018, which could result in changes in the valuation of our deferred tax asset and liabilities. Any such change in valuation could have a material impact on our income tax expense and deferred tax balances.

The TCJA is a far-reaching and complex revision to the U.S. federal income tax laws with disparate and, in some cases, countervailing impacts on different categories of taxpayers and industries, and will require subsequent rulemaking and interpretation in a number of areas. The long-term impact of the TCJA on the overall economy, the industries in which we operate and our partners businesses cannot be reliably predicted at this early stage of the new law’s implementation. There can be no assurance that the TCJA will not negatively impact our operating results, financial condition, and future business operations. The estimated impact of the TCJA is based on our management’s current knowledge and assumptions, following consultation with our tax advisors. Recognized impacts could be materially different from current estimates based on our actual results and our further analysis of the new law. The impact of the TCJA on holders of common stock is uncertain and could be materially adverse. This Annual Report

does not discuss any such tax legislation or the manner in which it might affect investors in common stock. Investors should consult with their own tax advisors with respect to such legislation and the potential tax consequences of investing in common stock.

New legislation or regulation which could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments which could have a negative impact on our financial results. Additionally, we use our best judgment in attempting to quantify and provide for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions may cause actual financial results to deviate from previous estimates.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the foreseeable future and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. We may be unable to use these losses to offset income before such unused losses expire. Under Sections 382 and

383 of the Code, utilization of net operating losses and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred or that could occur in the future. In general, an “ownership change” as defined by Section 382 of the Code results from a transaction or series of transactions over a three year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders. We have in the past experienced ownership changes that have resulted in limitations on the use of a portion of our net operating loss carryforwards. We have completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since our formation. The results of this study indicated we experienced ownership changes, as defined by Section 382 of the Code, in each of 2006, 2011, 2012, 2013 and 2016 resulting in limitations on the use of a portion of our net operating loss carryforwards.. If we experience further ownership changes, our ability to utilize our net operating loss carryforwards could be further limited.

Our internal computer systems, or those of our development partners, third-party clinical research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our development partners, third-party clinical research organizations, data management organizations and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for any of our product candidates 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 results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

We rely on email and other messaging services in connection with our operations. We may be targeted by parties using fraudulent spoofing and phishing emails to misappropriate passwords, payment information or other personal information or to introduce viruses through Trojan horse programs or otherwise through our networks, computers, smartphones, tablets or other devices. Despite our efforts to mitigate the effectiveness of such malicious email campaigns through a variety of control and non-electronic checks, spoofing and phishing may damage our business and increase our costs. We do not currently maintain a cyber insurance policy. Any of these events or circumstances could materially adversely affect our business, financial condition and operating results.

We use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly. We may incur significant costs complying with environmental laws and regulations.

Our research and development and manufacturing processes involve the controlled use of hazardous materials, including chemicals and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our insurance coverage and our total assets. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials and specified waste products, as well as the discharge of pollutants into the environment and human health and safety matters.

Compliance with environmental laws and regulations may be expensive and may impair our research, development and production efforts. If we fail to comply with these requirements, we could incur substantial costs, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes

necessary to achieve and maintain compliance. In addition, we cannot predict the impact on our business of new or amended environmental laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced.

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

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA or foreign regulators, failure to provide accurate information to regulatory authorities, failure to comply with manufacturing standards we have established, failure to comply with federal and state health care fraud and abuse laws and regulations in the United States and abroad, failure to report financial information or data accurately, disclose unauthorized activities to us or failure to comply with our own internal company policies. 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. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to 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.

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

Costs associated with being a public reporting company are significant, and public reporting requirements divert significant company resources and management attention.

We are subject to the reporting requirements of the Exchange Act and the other rules and regulations of the SEC. We are working with our legal, independent accounting and financial advisors to identify those areas in which changes should be made to our financial and management control systems to manage our growth and our obligations as a public reporting company including preparing for the commercialization of NeoCart, if approved. These areas include corporate governance, corporate control, disclosure controls and procedures, and financial reporting and accounting systems. We have made, and will continue to make, changes in these and other areas. Compliance with the various reporting and other requirements applicable to public reporting companies will require considerable time, attention of management and financial resources. In addition, the changes we make may not be sufficient to allow us to satisfy our obligations as a public reporting company on a timely basis.

Further, the listing requirements of Nasdaq require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve as our directors or executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms.

Our business is subject to the risks of earthquakes, fire, power outages, floods and other catastrophic events, and to interruption by manmade problems such as terrorism. If any of our manufacturing, processing or storage facilities are damaged or destroyed, our business and prospects would be adversely affected.

A significant natural disaster, such as an earthquake, fire or flood, or a significant power outage, could have a material adverse impact on our business, operating results and financial condition. If any of our manufacturing, processing or storage facilities, or any of the equipment in such facilities were to be damaged or destroyed, this would force us to delay or halt our clinical trial or commercial production processes. We currently produce materials for our clinical trials at our manufacturing facilities located in Waltham, Massachusetts, and we produce our critical raw materials for use in NeoCart production in our facilities located in Lexington, Massachusetts. If these facilities or the equipment in them are significantly damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity. In addition, natural disasters could affect our third-party service providers’ and manufacturers ability to perform services and provide materials for us on a timely basis. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, our efforts to obtain regulatory approvals for, and to commercialize, our product candidates may be delayed or prevented. For example, if natural weather or disasters were to interrupt air travel, our NeoCart implants may not be delivered to patients before expiry resulting in a loss of

product and a related financial loss as well as the potential loss of a customer. In addition, acts of terrorism could cause disruptions in our business or the business of our third-party service providers, partners, customers or the economy as a whole.

We are increasingly dependent on information technology systems, infrastructure and data.

We are increasingly dependent upon information technology systems, infrastructure and data. Our computer systems may be vulnerable to service interruption or destruction, malicious intrusion and random attack. Security breaches pose a risk that sensitive data, including intellectual property, clinical data, trade secrets or personal information may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, denial-of service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our key business partners face similar risks, and a security breach of their systems could adversely affect our security posture. While we continue to invest data protection and information technology, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information or the illegal transfer of funds to unknown persons, which could result in financial, legal, business or reputational harm.

Risks Related to Regulatory Approval

If we fail to complete clinical trials and obtain regulatory approval for NeoCart, our business would be significantly harmed.

We have not completed clinical development for any of our product candidates and will only obtain regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities in well-designed and conducted clinical trials that the product candidate is safe, effective, and otherwise meets the appropriate standards required for approval for a particular class of products or indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain results. A failure of one or more clinical trials may occur at any stage. Of the large number of products in development, only a small percentage successfully complete the FDA regulatory approval process and are commercialized.

We have never obtained marketing approval from the FDA or any comparable foreign regulatory authority for NeoCart or any of our products in the recent past. Our ability to obtain regulatory approval of our product candidates depends on, among other things, whether our clinical trials demonstrate statistically significant efficacy with safety issues that do not potentially outweigh the therapeutic benefit of the product candidates, and whether the regulatory agencies agree that the data from our future clinical trials is sufficient to support approval for any of our product candidates. The final results of our current and future clinical trials may not meet the FDA's or other regulatory agencies' requirements to approve a product candidate for marketing, and the regulatory agencies may otherwise determine that our manufacturing processes, comparability data for our critical raw materials, or facilities are insufficient to support approval. We may need to conduct more clinical trials than we currently anticipate. Even if we do receive FDA or other regulatory agency approval, we may not be successful in commercializing approved product candidates. If any of these events occur, our business could be materially harmed and the value of our common stock would likely decline.

Our clinical development of NeoCart could be substantially delayed if the FDA requires us to conduct additional studies or trials or imposes other requirements or restrictions.

We will need to generate and provide the FDA with comparability data from our new raw material production for the critical raw materials used in our manufacturing process and intended for commercial use. The FDA may also require us to generate additional preclinical or clinical data to support the use of these new critical raw material supplies prior to commercialization, if any, and may require additional clinical data in order to accept the BLA submission. These additional requirements may cause delays in our NeoCart development program which could require us to incur additional development costs, seek funding for these increased costs or delay or cease our clinical development and BLA submission activities for NeoCart. Any inability to advance NeoCart or any other product candidate through clinical development would have a material adverse effect on our business.

We expect to conduct an additional study in pediatric patients if NeoCart is approved. The Food and Drug Administration Safety and Innovation Act made permanent the Pediatric Research Equity Act, which requires a sponsor to conduct pediatric studies for most tissue regeneration products for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under the Pediatric Research Equity Act, original NDAs and BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations, and it is likely that we will negotiate with FDA the terms of such a deferral. A deferral may be granted for several reasons, including a finding that the tissue regeneration products is ready for approval for use in adults before pediatric studies are initiated or completed or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to

submit a request for approval of a pediatric formulation.

We are subject to numerous U.S. federal and state laws pertaining to health care fraud and abuse, including anti-kickback, self-referral, false claims and fraud laws, and any violation by us of such laws could result in fines or other penalties.

If one or more of our product candidates is approved, we will be subject to U.S. federal and state laws intended to prevent health care fraud and abuse. The federal anti-kickback statute prohibits the offer, receipt, or payment of remuneration in exchange for or to induce the referral of patients or the use of products or services that would be paid for in whole or part by Medicare, Medicaid or other federal health care programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. Many states have similar laws that apply to their state health care programs as well as private payors. Violations of the anti-kickback laws can result in exclusion from federal health care programs and substantial civil and criminal penalties.

The False Claims Act imposes liability on persons who, among other things, present or cause to be presented false or fraudulent claims for payment by a federal health care program. The False Claims Act has been used to prosecute persons submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. The False Claims Act includes a whistleblower provision that allows individuals to bring actions on behalf of the federal government and share a portion of the recovery of successful claims. If our marketing or other arrangements were determined to violate the False Claims Act or anti-kickback or related laws, then our revenue could be adversely affected, which would likely harm our business, financial condition and results of operations.

State and federal authorities have aggressively targeted medical technology companies for alleged violations of these anti-fraud statutes, based on improper research or consulting contracts with doctors, certain marketing arrangements that rely on volume-based pricing, off-label marketing

schemes and other improper promotional practices. Companies targeted in such prosecutions have paid substantial fines in the hundreds of millions of dollars or more, have been forced to implement extensive corrective action plans or Corporate Integrity Agreements, and have often become subject to consent decrees severely restricting the manner in which they conduct their business. If we become the target of such an investigation or prosecution based on our contractual relationships with providers or institutions, or our marketing and promotional practices, we could face similar sanctions, which would materially harm our business.

The Foreign Corrupt Practices Act and similar worldwide anti-bribery laws generally prohibit companies and their intermediaries from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. We cannot assure you that our internal control policies and procedures will protect us from reckless or negligent acts committed by our employees, future distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations and reputation.

Also, the Physician Payment Sunshine Act imposes new reporting and disclosure requirements on drug, device, biologic and medical supply manufacturers for any “transfer of value” made or distributed to prescribers and other healthcare providers. In addition, device and drug manufacturers will also be required to report and disclose any investment interests held by physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in significant civil monetary penalties.

Our failure to comply with extensive governmental regulation may significantly affect our operating results.

Even if we obtain regulatory approval for some or all of our product candidates, we will continue to be subject to extensive ongoing requirements by the FDA, as well as by a number of foreign, national, state and local agencies.

These regulations will impact many aspects of our operations, including testing, research and development, manufacturing, safety, efficacy, labeling, storage, quality control, adverse event reporting, import and export, record keeping, approval, distribution, advertising and promotion of our future products. We must also submit new or supplemental applications and obtain FDA approval for certain changes to an approved product, product labeling or manufacturing process. Application holders must also submit advertising and other promotional material to the FDA and report on ongoing clinical trials. The FDA enforces post-marketing regulatory requirements, including cGMP requirements, through periodic unannounced inspections. We do not know whether we will pass any future FDA inspections. Failure to pass an inspection could disrupt, delay or shut down our manufacturing operations. Failure to comply with applicable regulatory requirements could, among other things, result in:

- administrative or judicial enforcement actions;
- changes to advertising;
- failure to obtain marketing approvals for our product candidates;
- revocation or suspension of regulatory approvals of products;
- product seizures or recalls;
- court-ordered injunctions;
- import detentions;
- delay, interruption or suspension of product manufacturing, distribution, marketing and sales; or
- civil or criminal sanctions.

The discovery of previously unknown problems with our product candidates or future products may result in restrictions of the products, including withdrawal from the market. In addition, the FDA may revisit and change its prior determinations with regard to the safety or efficacy of our future products. If the FDA’s position changes, we may be required to change our labeling or cease to manufacture and market our future products.

Even prior to any formal regulatory action, we could voluntarily decide to cease the distribution and sale or recall any of our future products if concerns about their safety or efficacy develop.

In their regulation of advertising and other promotion, the FDA and the U.S. Federal Trade Commission may issue correspondence alleging that some advertising or promotional practices are false, misleading or deceptive. The FDA and the U.S. Federal Trade Commission are authorized to impose a wide array of sanctions on companies for such advertising and promotion practices, which could result in any of the following:

- our incurrence of substantial expenses, including fines, penalties, legal fees and costs to comply with the FDA's requirements;
- our being required to change in the methods of marketing and selling products;
- our being required to take FDA mandated corrective action, which may include placing advertisements or sending letters to physicians rescinding previous advertisements or promotions; or
- a disruption in the distribution of products and loss of sales until compliance with the FDA's position is obtained.

Improper promotional activities may also lead to investigations by federal or state prosecutors, and result in criminal and civil penalties. If we become subject to any of the above requirements, it could be damaging to our reputation and restrict our ability to sell or market our future products, and our business condition could be adversely affected. We may also incur significant expenses in defending ourselves.

Physicians may prescribe pharmaceutical or biologic products for uses that are not described in a product's labeling or differ from those tested by us and approved by the FDA. While such "off-label" uses are common and the FDA does not regulate physicians' choice of treatments, the FDA does restrict a manufacturer's communications on the subject of off-label use. Companies cannot promote FDA-approved pharmaceutical or biologic products for off-label uses, but under certain limited circumstances they may disseminate to practitioners' articles published in peer-reviewed journals. To the extent allowed by the FDA, we intend to disseminate peer-reviewed articles on our future products to practitioners. If, however, our activities fail to comply with the FDA's regulations or guidelines, we may be subject to warnings from, or enforcement action by, the FDA or other regulatory or law enforcement authorities.

Depending on the circumstances, failure to meet post-approval requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal 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.

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, qualification testing, post-approval clinical data, labeling and promotional activities for such product, will be subject to continuing and additional requirements of the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information, reports, facilities registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of pharmaceutical and biological products to ensure such products are marketed only for the approved indications and in accordance with the provisions of the approved labeling.

In addition, later discovery of previously unknown problems with our products, manufacturing processes, or failure to comply with regulatory requirements, may lead to various adverse results, including:

- restrictions on such products, manufacturers, facilities or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
    - requirements to conduct post-marketing clinical trials;
- requirements to institute a risk evaluation and mitigation strategy to monitor safety of the product post-approval;
- warning letters issued by the FDA or other regulatory authorities;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recalls of products, fines, restitution or disgorgement of profits or revenue;
- suspension, revocation or withdrawal of marketing approvals;
- refusal to permit the import or export of our products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates or future facilities expansions. 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, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will

afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to these product candidates could have a material adverse effect on our financial condition and results of operations.

Composition-of-matter patents are generally considered to be the strongest form of intellectual property protection as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition-of-matter of our product candidates will be considered patentable by the U.S. Patent and Trademark Office and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for a use that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- The U.S. Patent and Trademark Office and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.
- Patent applications may not result in any patents being issued.
- Patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or otherwise may not provide any competitive advantage.
- Our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use and sell our potential product candidates.
- There may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for treatments that prove successful, as a matter of public policy regarding worldwide health concerns.
- Countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, third parties may still obtain this information or may come upon this or similar information independently. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

If we or any of our future development or collaborative partners are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation could have a material adverse effect on our business.

Our success also depends on our ability and the ability of our current or future development or collaborative partners to develop, manufacture, market and sell our product candidates without infringing upon the proprietary rights of third parties. Numerous U.S. and foreign-issued patents and pending patent applications owned by third parties exist in the fields in which we are developing product candidates, some of which may contain claims that overlap with the subject matter of our intellectual property or are directed at our product candidates, technologies or methods of manufacture. When we become aware of patents held by third parties that may implicate the manufacture, development or commercialization of our product candidates, we evaluate our need to license rights to such patents. If we need to license rights from third parties to manufacture, develop or commercialize our product candidates, there can be no assurance that we will be able to obtain a license on commercially reasonable terms or at all.

Because patent applications can take many years to issue there may be currently pending applications, unknown to us, that may later result in issued patents upon which our product candidates or proprietary technologies may infringe. Similarly, there may be issued patents relevant to our product candidates of which we are not aware.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biologics industry generally. If a third-party claims that we or any of our licensors, suppliers or development partners infringe upon a third-party's intellectual property rights, we may have to:

- seek to obtain licenses that may not be available on commercially reasonable terms, if at all;
- abandon an infringing product candidate or redesign our products or processes to avoid infringement;
- pay substantial damages including, in an exceptional case, treble damages and attorneys' fees, which we may have to pay if a court decides that the product candidate or proprietary technology at issue infringes upon or violates the third-party's rights;
- pay substantial royalties or fees or grant cross-licenses to our technology; or
- defend litigation or administrative proceedings that may be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Third parties may infringe upon our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, found to be unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

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

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

Our issued patents could be found invalid or unenforceable if challenged in court which could have a material adverse effect on our business.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates or one of our future product candidates, technologies or methods of manufacture, the defendant could counterclaim that our patent 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 or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. Patent and Trademark Office, or made a misleading statement, during prosecution. Third parties may also raise similar claims before the U.S. Patent and Trademark Office even outside the context of litigation. 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 we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

56

We may be subject to claims that our consultants or independent contractors have wrongfully used or disclosed alleged trade secrets of their other clients or former employers to us, which could subject us to costly litigation.

As is common in the biotechnology industry, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants were previously employed at, or may have previously or may be currently providing consulting services to, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may become subject to claims that our company or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve technological and legal complexity. Therefore, obtaining and enforcing biotechnology patents is costly, time consuming and inherently uncertain. In addition, Congress recently passed patent reform legislation. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the U.S. Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world which could materially, negatively affect our business.

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 can be less extensive than those in the United States. 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. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, 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 have not 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 and other intellectual property protection, particularly those relating to biotechnology, 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 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 and may adversely affect our business.

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.

Our registered or unregistered 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 by potential partners or customers in our markets of interest. 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.

Risks Related to Our Common Stock

The trading price of our common stock has been, and is likely to continue to be, volatile, and you might not be able to sell your shares at or above the price you paid.

Our stock price has been and will likely continue to be volatile for the foreseeable future. The realization of any of the risks described in these risk factors or other unforeseen risks could have a dramatic and adverse effect on the market price of our common stock. The trading price of our common stock is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed elsewhere in this “Risk Factors” section and others such as:

- the delay or failure of our ability to submit a BLA to the FDA or secure regulatory approvals for NeoCart in a timely manner;

- any additional data or results from our NeoCart Phase 3 clinical trial in the U.S. or clinical trials in Japan conducted by our partners, and the results of trials of our competitors or those of other companies in our market sector;
- the delay or failure in initiating, enrolling or completing preclinical studies or clinical trials, or unsatisfactory results of these trials;
- announcements about us or about our competitors including clinical trial results, regulatory approvals, or new product candidate introductions and the revenue and growth potential of such new products;
- developments concerning our current or future development partners, licensors or product candidate manufacturers;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the pharmaceutical or biotechnology industries, regulations or concerns related to cell and gene therapies, and the economy as a whole;
- governmental regulation and legislation;
- the recruitment or departure of members of our board of directors, management team or other key personnel;
- changes in our operating results;
    - any changes in the financial projections we may provide to the public, our failure to meet these projections, or changes in recommendations by any securities analysts that elect to follow our common stock;
- any change in securities analysts' estimates of our performance, or our failure to meet analysts' expectations;
- the expiration of market standoff or contractual lock-up agreements;
- sales or potential sales of substantial amounts of our common stock; and
- price and volume fluctuations in the overall stock market or resulting from inconsistent trading volume levels of our shares.

In recent months and years, the stock market in general, and the market for pharmaceutical and biotechnological companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. In addition, Brexit or actions taken by the new presidential administration and Congress could adversely affect United States, European or worldwide economic or market conditions and could contribute to instability and volatility in global financial markets. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance.

Our quarterly operating results may fluctuate substantially, which may cause the price of our common stock to fluctuate substantially.

We expect our quarterly operating results to be subject to fluctuations. Our net income or loss and other operating results may be affected by numerous factors, including:

- variations in the level of expenses related to our BLA preparation, any additional clinical trials or data required by the FDA prior to approval of NeoCart and potential commercialization activities for NeoCart;
- any variations in the level of expenses related to our development and expected manufacturing and commercialization of NeoCart;
- derivative instruments recorded at fair value, including but not limited to the change in fair value of warrants issued in connection with a private placement we completed in 2016 and warrants issued in our 2018 public offering;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
    - the addition or termination of any clinical trials;
- further development of future product candidates or post-marketing requirements for NeoCart
- any regulatory or clinical developments affecting NeoCart;
- the nature and terms of any stock-based compensation grants and any intellectual property infringement lawsuits in which we may become involved; and
- market acceptance of NeoCart upon FDA approval, if at all, and expectations regarding sales of NeoCart following such approval, if at all.

58

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our stock price may continue to be volatile, and securities class action litigation has often been instituted against companies following periods of volatility of their stock price. Any such litigation, if instituted against us, could result in substantial costs and a diversion of our management's attention and resources.

In the past, following periods of volatility in the overall market and the market price of a particular company's securities, securities class action litigation has often been instituted against these companies. This litigation, if instituted against us, could result in substantial costs and a diversion of our management's attention and resources.

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

The trading market for our common stock will depend in part on the research and reports that securities and industry analysts publish about us or our business. In the event we obtain additional securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our stock or publishes unfavorable research about our business, or if our clinical trials or operating results fail to meet the analysts' expectations, our stock price would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Raising additional funds by issuing securities or through licensing or lending arrangements may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights.

We will need to raise additional funding in order to gain any regulatory approval of NeoCart, create additional manufacturing capacity and to commercialize NeoCart and to conduct the research and development and clinical and regulatory activities necessary to bring other product candidates to market. To the extent that we raise additional capital by issuing equity securities, the share ownership of existing stockholders will be diluted. Any future debt financing may involve covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments, and engage in certain merger, consolidation, or asset sale transactions. In addition, if we seek funds through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us.

We have never paid and do not intend to pay cash dividends and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never paid cash dividends on any of our capital stock, and we currently intend to retain future earnings, if any, to fund the development and growth of our business. Therefore, you are not likely to receive any dividends on our common stock for the foreseeable future or at all. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which you have purchased it.

Our principal stockholders and management own a significant percentage of our stock and may be able to exert significant control over matters subject to stockholder approval.

As of November 6, 2018, our executive officers, directors, holders of more than 5% of our capital stock and their respective affiliates beneficially owned approximately 29.1% of our outstanding capital stock. These stockholders may have the ability to influence us through their ownership position. These stockholders are able to determine all

matters requiring stockholder approval. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Substantial future sales of shares by existing stockholders, including pursuant to our equity incentive plans, or the perception that such sales may occur, could cause our stock price to decline.

A small number of institutional investors and private equity funds hold a significant number of shares of our common stock and all of our shares of Series A Convertible Preferred Stock and warrants to purchase our common stock issued in our September 2016 private placement and October 2018 public offering. If these existing stockholders, particularly our directors and executive officers and the venture capital funds affiliated with our current and former directors, sell substantial amounts of our common stock in the public market, or are perceived by the public market as intending to sell substantial amounts of our common stock, the trading price of our common stock could decline.

Some of pre-IPO existing security holders have demand and piggyback rights to require us to register with the SEC up to 4,479,418 shares of our common stock. If we register these shares of common stock, the stockholders would be able to sell those shares freely in the public market,

subject to Rule 144 transfer restrictions applicable to affiliates. In November 2016, we registered 26,800,001 shares of common stock for resale by selling stockholders, including 10,737,275 shares of common stock underlying our outstanding Series A Convertible Preferred Stock and 13,466,667 shares of common stock underlying outstanding warrants issued in connection with our September 2016 private placement. The selling stockholders in the private placement are able to freely trade such shares of common stock, subject to Rule 144 transfer restrictions applicable to affiliates. We have registered an additional 3,471,339 shares of our common stock that we may issue under our equity plans. Once we issue these shares, they can be freely sold in the public market upon issuance, contractual lock-up agreements or Rule 144 transfer restrictions applicable to affiliates.

We received a deficiency letter in October 2018 the Nasdaq Listing Qualifications Department (the "Staff") of the Nasdaq Stock Market LLC ("Nasdaq") notifying the Company that, for the last 30 consecutive business days, the closing bid price for the Company's common stock had closed below a minimum $1.00 per share required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2). If we were to fail to regain compliance, our shares could be delisted from the Nasdaq Capital Market, which could materially reduce the liquidity of our common stock and have an adverse effect on its market price.

On October 17, 2018, we received a deficiency letter from the Staff notifying us that, for the 30 consecutive business days prior to October 17, 2018, the closing bid price for our common stock had closed below a minimum $1.00 per share required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2) ("Rule 5550(a)(2)"). The Nasdaq deficiency letter has no immediate effect on the listing of our common stock, and our common stock will continue to trade on The Nasdaq Capital Market under the symbol "HSGX" at this time.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we have been given 180 calendar days, or until April 15, 2019 to regain compliance with Rule 5550(a)(2). If we choose to implement a reverse stock split, we must complete the split no later than ten business days prior to April 15, 2019 to regain compliance. If at any time before April 15, 2019, the bid price of our common stock closes at $1.00 per share or more for a minimum of 10 consecutive business days (an "Automatic Compliance Event"), the Staff will provide written confirmation that we have achieved compliance with Rule 5550(a)(2).

If we do not regain compliance with Rule 5550(a)(2) by April 15, 2019, we may be afforded a second 180 calendar day period to regain compliance. To qualify, we would be required to meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, except for the minimum bid price requirement. In addition, we would be required to notify Nasdaq of our intent to cure the deficiency during the second compliance period, which may include, if necessary, implementing a reverse stock split.

If we do not regain compliance with Rule 5550(a)(2) by April 15, 2019, and we are not eligible for an additional compliance period at that time, the Staff will provide notice to us that our securities will be subject to delisting. At that time, we may appeal the Staff's delisting determination to a Nasdaq Listing Qualifications Panel ("Panel"). We would remain listed pending the Panel's decision.

A delisting would also likely make it more difficult for us to obtain financing through the sale of our equity. Any such sale of equity would likely be more dilutive to our current stockholders than would be the case if our shares were listed.

We may not satisfy The Nasdaq Capital Market's other requirements for continued listing. If we cannot satisfy these requirements, Nasdaq could delist our common stock.

Our common stock is listed on The Nasdaq Capital Market under the symbol "HSGX". To continue to be listed on Nasdaq, we are required to satisfy a number of conditions. Other than the deficiency letter discussed in the immediately prior risk factor, we previously received two letters from Nasdaq, with the first letter in November 2016 notifying us of our failure to maintain a minimum market value of listed securities of $50,000,000 for the 30

consecutive business days. We subsequently regained compliance with this listing standard in March 2017. The second letter in May 2017 notified us of our failure to maintain a minimum of $10,000,000 in stockholders' equity as required for companies trading on The Nasdaq Global Market. In response to the second letter, we transferred our securities to The Nasdaq Capital Market in June 2017 to regain compliance with the minimum stockholders' equity requirement.

We cannot assure you that we will be able to satisfy the Nasdaq listing requirements in the future. If we are delisted from Nasdaq, trading in our shares of common stock may be conducted, if available, on the "OTC Bulletin Board Service" or, if available, via another market. In the event of such delisting, an investor would likely find it significantly more difficult to dispose of, or to obtain accurate quotations as to the value of the shares of our common stock, and our ability to raise future capital through the sale of the shares of our common stock or other securities convertible into or exercisable for our common stock could be severely limited. A determination could also then be made that our common stock is a "penny stock" which would require brokers trading in our common stock to adhere to more stringent rules and possibly result in a reduced level of trading. This could have a long-term impact on our ability to raise future capital through the sale of our common stock.

We may seek authorization to issue additional shares of common stock to continue to have the ability to raise capital in the capital markets to finance our existing business plans and to potentially effect a reverse stock split in order to maintain compliance with applicable Nasdaq rules.

The Company may hold a Special Meeting for the holders of record of the Company's common stock(the "Special Meeting"). The proposals which may be voted upon at the Special Meeting would be to (i) approve an amendment to our Sixth Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") to increase the Company's authorized shares of Common Stock from 100,000,000 to 250,000,000 (the "Authorized Share Increase") and (ii) approve an amendment to the Certificate of Incorporation, to effect a reverse stock split of our outstanding Common Stock at a ratio between 1-for-2 and 1-for-20, to be determined at the discretion of the Company's Board of Directors (the "Board") at any time before the earlier of June 30, 2019 and the next annual meeting of stockholders of the Company, for the purpose of complying with Nasdaq Listing Rule 5550(a)(2), subject to the Board's discretion to abandon such amendment (the "Reverse Split"). Proxies for the Special Meeting will be mailed to stockholders if the Company determines it will seek approval of such matters.

At the time that we may need additional financing, we may not have sufficient authorized shares of common stock available, depending on the amount of the financing, the price of our common stock and our obligations to reserve shares for our outstanding convertible preferred stock, warrants and options. As of October 15, 2018, we had outstanding 62,025,398 shares of Common Stock. Additionally, we have reserved (i) 3,655,578 shares of Common Stock issuable upon the exercise of outstanding options under our equity incentive plans, (ii) 148,613 shares of Common Stock reserved for issuance under the 2013 Plan, (iii) 33,145,228 shares of Common Stock issuable upon the exercise of outstanding warrants, (iv) 177,996 shares of Common Stock issuable upon conversion of shares of our Series A Convertible Preferred Stock, (v) 361,973 shares of Common Stock reserved for issuance under our 2013 Employee Stock Purchase Plan and (vi) 200,000 shares of Common Stock reserved for issuance under an inducement option granted outside of the 2013 Plan pursuant to Nasdaq Listing Rule 5635(c)(4). As a result, we have allocated 99,566,173 shares of our 100,000,000 shares of authorized Common Stock under the Certificate of Incorporation, leaving only 591,599 shares of Common Stock unallocated for potential issuance. To increase our authorized common stock, we would need stockholder approval to amend the Certificate of Incorporation, which approval may not be obtained. Implementation of the Reverse Stock split would increase the shares available for issuance without increasing our authorized shares.

If sought, the stockholders may or may not approve the Authorized Share Increase and/or the Reverse Split. In the event that the Authorized Share Increase and/or the Reverse Split are not approved, the Company may have to adjourn the Special Meeting to seek additional votes in support of one or both of the proposals or explore other methods to increase its authorized capital or to raise capital in the capital markets in order to operate and fund the business plans of the Company, including the potential issuance and sale of some or all of the Company's remaining authorized common stock and/or preferred stock. If the Company is not able to increase its shares of authorized common stock, it may be unable to operate or to finance its business plan. We cannot guarantee that the Reverse Split will be successfully implemented or, if it is successfully implemented, that the closing market price of our common stock will not decline further.

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

Our certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit the board of directors to establish the number of directors;

- provide that directors may only be removed "for cause";
- require super-majority voting to amend some provisions in our certificate of incorporation and bylaws;
- authorize the issuance of "blank check" preferred stock that our board of directors could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- provide that the board of directors is expressly authorized to make, alter or repeal our bylaws; and
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on merger, business combinations and other transactions between us and holders of 15% or more of our common stock.

We are an emerging growth company and the extended transition period for complying with new or revised financial accounting standards and reduced disclosure and governance requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are an emerging growth company. Under the Jumpstart Our Business Startups Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We plan to avail ourselves of this exemption from new or revised accounting standards and, therefore, we may not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

For as long as we continue to be an emerging growth company, we also intend to take advantage of certain other exemptions from various reporting requirements that are applicable to other public companies, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory stockholder vote on executive compensation and any golden parachute payments not previously approved, exemption from the requirement of auditor attestation on our internal control over financial reporting and exemption from 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 (auditor discussion and analysis). If we do, the information that we provide stockholders may be different than what is available with respect to other public companies.

Investors could find our common stock less attractive because we will rely on these exemptions, which may make it more difficult for investors to compare our business with other companies in our industry. 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, it may be difficult for us to raise additional capital as and when we need it. If we are unable to do so, our financial condition and results of operations could be materially and adversely affected.

We will remain an emerging growth company until the earliest of: (1) the end of the fiscal year in which the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the end of the second fiscal quarter; (2) the end of the fiscal year in which we have total annual gross revenue of $1.0 billion or more during such fiscal year; (3) the date on which we issue more than $1.0 billion in non-convertible debt in a three-year period or (4) December 31, 2019, the end of the fiscal year following the fifth anniversary of the completion of our initial public offering.

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

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Exhibit	Description
3.1	Sixth Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K as filed on December 8, 2014, and incorporated herein by reference)
3.2	Amended and Restated Bylaws (filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K as filed on December 8, 2014, and incorporated herein by reference)
31.1*	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of the Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002
32.1*	Certifications of the Chief Executive Officer and Chief Financial Officer as required by 18 U.S.C. 1350
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

*Filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Histogenics Corporation

Dated: November 8, 2018 /s/ Adam Gridley
Adam Gridley
President and Chief Executive Officer

(Principal Executive Officer)

Dated: November 8, 2018 /s/ Jonathan Lieber
Jonathan Lieber
Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)