# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 10-Q

**(Mark One)**

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

**FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2021**

**OR**

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

**FOR THE TRANSITION PERIOD FROM _____ TO _____**

**Commission File Number 000-22873**

# ARCA BIOPHARMA, INC.

**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **36-3855489** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(I.R.S. Employer Identification Number)** |
| **10170 Church Ranch Way, Suite 100, Westminster, CO** | **80021** |
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**(720) 940-2200**
**(Registrant's Telephone Number, including Area Code)**

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

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, par value $0.001 per share | ABIO | Nasdaq Capital Market |

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

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

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

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

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

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

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

| **Class** | **Number of Shares Outstanding** |
|---|---|
| Common Stock, par value $0.001 per share | On November 1, 2021: 14,410,143 |

**ARCA BIOPHARMA, INC.**
**FORM 10-Q**
**FOR THE QUARTER ENDED SEPTEMBER 30, 2021**

**PART I. FINANCIAL INFORMATION**

**ITEM 1. FINANCIAL STATEMENTS**

**ARCA BIOPHARMA, INC.**
**BALANCE SHEETS**
**(Unaudited)**

| | September 30, 2021 | December 31, 2020 |
|---|---|---|
| | (in thousands, except share and per share amounts) | |
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 58,313 | $ 49,071 |
| Other current assets | 1,353 | 897 |
| Total current assets | 59,666 | 49,968 |
| Right-of-use asset - operating | 460 | 428 |
| Property and equipment, net | 48 | 21 |
| Other assets | 18 | 12 |
| **Total assets** | $ 60,192 | $ 50,429 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,131 | $ 1,773 |
| Accrued compensation and employee benefits | 146 | 815 |
| Accrued expenses and other liabilities | 1,905 | 911 |
| Total current liabilities | 3,182 | 3,499 |
| Operating lease liability, net of current portion | 410 | 409 |
| **Total liabilities** | 3,592 | 3,908 |
| Commitments and contingencies | | |
| **Stockholders' equity:** | | |
| Common stock, $0.001 par value; 100 million shares authorized at September 30, 2021 and December 31, 2020; 14,410,143 and 9,548,150 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively | 14 | 10 |
| Additional paid-in capital | 224,386 | 200,665 |
| Accumulated deficit | (167,800) | (154,154) |
| **Total stockholders' equity** | 56,600 | 46,521 |
| **Total liabilities and stockholders' equity** | $ 60,192 | $ 50,429 |

See accompanying Notes to Financial Statements

**ARCA BIOPHARMA, INC.**

**STATEMENTS OF OPERATIONS**
**(unaudited)**

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2021 | 2020 | 2021 | 2020 |
| | (in thousands, except share and per share amounts) | | | |
| Costs and expenses: | | | | |
| Research and development | $ 3,438 | $ 1,051 | $ 9,891 | $ 1,788 |
| General and administrative | 1,278 | 939 | 3,764 | 2,852 |
| Total costs and expenses | 4,716 | 1,990 | 13,655 | 4,640 |
| Loss from operations | (4,716) | (1,990) | (13,655) | (4,640) |
| Interest and other income | 4 | 1 | 9 | 27 |
| Interest expense | — | (2) | — | (9) |
| Loss before income taxes | (4,712) | (1,991) | (13,646) | (4,622) |
| Income tax benefit | — | — | — | 9 |
| Net loss | $ (4,712) | $ (1,991) | $ (13,646) | $ (4,613) |
| Net loss per share: | | | | |
| Basic and diluted | $ (0.33) | $ (0.33) | $ (0.99) | $ (1.46) |
| Weighted average shares outstanding: | | | | |
| Basic and diluted | 14,410,143 | 6,044,315 | 13,733,259 | 3,154,680 |

See accompanying Notes to Financial Statements

**ARCA BIOPHARMA, INC.**

**STATEMENTS OF STOCKHOLDERS' EQUITY**
**(unaudited)**

| | Stockholders' Equity | | | | |
|---|---|---|---|---|---|
| | Common stock | | Additional Paid-In | Accumulated | |
| | Shares | Amount | Capital | Deficit | Total |
| | (in thousands, except share amounts) | | | | |
| **Balance, December 31, 2019** | **1,594,070** | **$ 2** | **$ 152,024** | **$ (144,416)** | **$ 7,610** |
| Share-based compensation | — | — | 16 | — | 16 |
| Net loss | — | — | — | (1,320) | (1,320) |
| **Balance, March 31, 2020** | **1,594,070** | **2** | **152,040** | **(145,736)** | **6,306** |
| Issuance of common stock and exercise of prefunded warrants for cash, net of offering costs | 673,500 | — | 5,297 | — | 5,297 |
| Share-based compensation | — | — | 4 | — | 4 |
| Net loss | — | — | — | (1,302) | (1,302) |
| **Balance, June 30, 2020** | **2,267,570** | **2** | **157,341** | **(147,038)** | **10,305** |
| Issuance of common stock for cash, net of offering costs | 7,018,054 | 7 | 42,129 | — | 42,136 |
| Share-based compensation | — | — | 5 | — | 5 |
| Net loss | — | — | — | (1,991) | (1,991) |
| **Balance, September 30, 2020** | **9,285,624** | **9** | **199,475** | **(149,029)** | **50,455** |
| Issuance of common stock for cash, net of offering costs | 262,526 | 1 | 1,172 | — | 1,173 |
| Share-based compensation | — | — | 18 | — | 18 |
| Net loss | — | — | — | (5,125) | (5,125) |
| **Balance, December 31, 2020** | **9,548,150** | **10** | **200,665** | **(154,154)** | **46,521** |
| Issuance of common stock for cash, net of offering costs | 4,861,993 | 4 | 23,343 | — | 23,347 |
| Share-based compensation | — | — | 141 | — | 141 |
| Net loss | — | — | — | (4,100) | (4,100) |
| **Balance, March 31, 2021** | **14,410,143** | **14** | **224,149** | **(158,254)** | **65,909** |
| Share-based compensation | — | — | 133 | — | 133 |
| Net loss | — | — | — | (4,834) | (4,834) |
| **Balance, June 30, 2021** | **14,410,143** | **14** | **224,282** | **(163,088)** | **61,208** |
| Share-based compensation | — | — | 104 | — | 104 |
| Net loss | — | — | — | (4,712) | (4,712) |
| **Balance, September 30, 2021** | **14,410,143** | **$ 14** | **$ 224,386** | **$ (167,800)** | **$ 56,600** |

See accompanying Notes to Financial Statements

**ARCA BIOPHARMA, INC.**

**STATEMENTS OF CASH FLOWS**
**(unaudited)**

| | Nine Months Ended September 30, | |
|---|---|---|
| | **2021** | **2020** |
| | (in thousands) | |
| **Cash flows from operating activities:** | | |
| Net loss | $ (13,646) | $ (4,613) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation | 11 | 6 |
| Amortization of right-of-use asset - operating | 52 | 71 |
| Share-based compensation | 378 | 25 |
| Change in operating assets and liabilities: | | |
| Other current assets | (439) | (281) |
| Other assets | (6) | (12) |
| Accounts payable | (405) | 83 |
| Accrued compensation and employee benefits | (670) | 92 |
| Accrued expenses and other liabilities | 910 | (101) |
| **Net cash used in operating activities** | (13,815) | (4,730) |
| **Cash flows from investing activities:** | | |
| Purchases of property and equipment | (36) | (6) |
| **Net cash used in investing activities** | (36) | (6) |
| **Cash flows from financing activities:** | | |
| Proceeds from the issuance of common stock | 24,070 | 49,644 |
| Common stock offering costs | (977) | (1,905) |
| Repayment of principal on vendor finance agreement | — | (271) |
| **Net cash provided by financing activities** | 23,093 | 47,468 |
| **Net increase in cash and cash equivalents** | 9,242 | 42,732 |
| Cash and cash equivalents, beginning of period | 49,071 | 8,363 |
| **Cash and cash equivalents, end of period** | $ 58,313 | $ 51,095 |
| Supplemental cash flow information: | | |
| Interest paid | $ — | $ 7 |
| Income tax refund received | $ — | $ 9 |
| Supplemental disclosure of noncash investing and financing transactions: | | |
| Leased assets obtained in exchange for operating lease liabilities | $ 84 | $ 49 |
| Purchases of property and equipment in accrued liabilities | $ 2 | $ — |
| Vendor finance agreement | $ — | $ 137 |
| Common stock offering costs accrued but not yet paid | $ — | $ 336 |
| Proceeds receivable from the issuance of common stock | $ — | $ 30 |

See accompanying Notes to Financial Statements

## (1) The Company and Summary of Significant Accounting Policies

### *Description of Business*

ARCA biopharma, Inc. (the Company or ARCA), a Delaware corporation, is headquartered in Westminster, Colorado. The Company is a clinical-stage biopharmaceutical company applying a precision medicine approach to the development and commercialization of genetically targeted therapies for cardiovascular diseases. The Company's lead product candidates are rNAPc2 (AB201) as a potential treatment for COVID-19, the disease caused by SARS-CoV-2 virus, and potentially other viral diseases and Gencaro™ (bucindolol hydrochloride) for the treatment of atrial fibrillation (AF) in patients with chronic heart failure (HF).

rNAPc2 is a protein therapeutic in clinical development as a potential treatment for patients hospitalized with COVID-19. Based on its unique mechanism of action, development history and the clinical evidence from the SARS-CoV-2 pandemic, the Company believes rNAPc2 has potential to be a beneficial therapy for patients with this serious viral disease. The Company initiated the Phase 2b clinical trial of rNAPc2 as a potential treatment for patients hospitalized with COVID-19 in the fourth quarter of 2020.

The Company continues to evaluate the feasibility and potential timing for initiating PRECISION-AF relative to the COVID-19 pandemic and prioritizing the development of rNAPc2.

The Company's other product candidate, AB171, is a thiol-substituted isosorbide mononitrate, which the Company believes could be developed as a genetically-targeted treatment for HF and peripheral arterial disease.

In March 2020, the World Health Organization declared the outbreak of COVID-19, a novel strain of Coronavirus, a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads. The Company does not expect a material financial effect as a result of the pandemic. However, if the pandemic continues to be a severe worldwide crisis, it could have a material adverse effect on the Company's business, results of operations, financial condition and cash flows.

### *Liquidity and Going Concern*

The Company devotes substantially all of its efforts towards clinical research and development, obtaining regulatory approval and raising capital necessary to fund its operations and it is subject to a number of risks associated with clinical research and development, including dependence on key individuals, the development of and regulatory approval of commercially viable products, the need to raise adequate additional financing necessary to fund the development and commercialization of its products, and competition from larger companies. The Company has not generated revenue to date and has incurred substantial losses and negative cash flows from operations since its inception. The Company has historically funded its operations through issuances of common and preferred stock.

The Company believes that its current cash and cash equivalents as of September 30, 2021 will be sufficient to fund its operations through the end of fiscal year 2022. Conducting a Phase 3 rNAPc2 clinical trial or the Phase 3 PRECISION-AF trial would likely require additional financing. However, changing circumstances may cause us to consume capital significantly faster or slower than currently anticipated. The Company has based these estimates on assumptions that may prove to be wrong, and the Company could exhaust its available financial resources sooner than the Company currently anticipates. Therefore, the Company may have to raise additional capital for clinical trials of rNAPc2 and will have to raise additional capital for clinical trials of Gencaro. The Company may not be able to raise sufficient capital on acceptable terms, or at all, to continue development of rNAPc2 or Gencaro or to otherwise continue operations and may not be able to execute any strategic transaction.

The Company's liquidity, and its ability to raise additional capital or complete any strategic transaction, depends on a number of factors, including, but not limited to, the following:

- the costs and timing for the potential additional clinical trials in order to gain possible regulatory approval for rNAPc2, Gencaro or any other product candidate;
- the market price of the Company's stock and the availability and cost of additional equity capital from existing and potential new investors;
- the Company's ability to retain the listing of its common stock on the Nasdaq Capital Market;
- general economic and industry conditions affecting the availability and cost of capital, including as a result of the COVID-19 pandemic;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the terms and conditions of the Company's existing collaborative and licensing agreements.

The sale of additional equity or convertible debt securities would likely result in substantial additional dilution to the Company's stockholders. If the Company raises additional funds through the incurrence of indebtedness, the obligations related to such indebtedness would be senior to rights of holders of the Company's capital stock and could contain covenants that would restrict the Company's operations. The Company also cannot predict what consideration might be available, if any, to the Company or its stockholders, in connection with any strategic transaction. Should strategic alternatives or additional capital not be available to the Company, or not be available on acceptable terms, the Company may be unable to realize value from its assets and discharge its liabilities in the normal course of business which may, among other alternatives, cause the Company to further delay, substantially reduce or discontinue operational activities to conserve its cash resources.

***Basis of Presentation***

The accompanying unaudited financial statements of the Company were prepared in accordance with generally accepted accounting principles for interim financial information and instructions to Form 10-Q and pursuant to Regulation S-X. Accordingly, these financial statements do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America (GAAP) for complete financial statements. In the opinion of management, these financial statements include all normal and recurring adjustments considered necessary for a fair presentation of these interim financial statements. The results of operations for the three and nine months ended September 30, 2021 are not necessarily indicative of results expected for the full year ending December 31, 2021. The Company has generated no revenue to date and its activities have consisted of seeking regulatory approval, research and development, exploring strategic alternatives for further developing and commercializing rNAPc2 and Gencaro, and raising capital. These unaudited financial statements should be read in conjunction with the audited financial statements and footnotes thereto for the year ended December 31, 2020 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission. Amounts presented are rounded to the nearest thousand, where indicated, except per share data and par values.

***Concentrations of Credit Risk***

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company has no off-balance-sheet concentrations of credit risk, such as foreign exchange contracts, option contracts, or foreign currency hedging arrangements. The Company maintains cash and cash equivalent balances in the form of bank demand deposits and money market fund accounts with financial institutions that management believes are creditworthy. Such balances may at times exceed the insured amount.

***Comprehensive Loss***

Comprehensive loss is defined as the change in equity during a period from transactions and other events and/or circumstances from non-owner sources. If the Company had comprehensive gains (losses), they would be reflected in the statement of operations and comprehensive loss and as a separate component in the statement of stockholders' equity. There were no elements of comprehensive loss during the three and nine months ended September 30, 2021 and 2020.

***Leases***

The Company determines if an arrangement is a lease at inception. Operating leases are included in right-of-use (ROU) asset – operating and lease obligations are included in accrued expenses and other liabilities and operating lease liability on the Company's September 30, 2021 and December 31, 2020 balance sheets.

ROU lease assets represent the Company's right to use an underlying asset for the lease term and lease obligations represent the Company's obligation to make lease payments arising from the lease. Operating ROU lease assets are recognized at the commencement date based on the present value of lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The Company's lease terms may include options to extend or terminate a lease when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

***Accrued Outsourcing Expenses***

As part of the process of preparing its financial statements, the Company is required to estimate accrued outsourcing expenses. This process involves identifying services that third parties have performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for these services as of the balance sheet date. Examples of estimated accrued outsourcing expenses include contract service fees, such as fees payable to contract manufacturers in connection with the production of materials related to the Company's drug product, and service fees and pass through costs from clinical research organizations. The Company develops estimates of liabilities using its judgment based upon the facts and circumstances known at the time.

***Recent Accounting Pronouncements***

The Company reviewed recently issued accounting pronouncements and concluded that they were either not applicable or not expected to have a significant impact to the financial statements.

**(2) Net Loss Per Share**

The Company calculates basic earnings per share by dividing net loss by the weighted average common shares outstanding during the period. Diluted earnings per share is computed by dividing net loss by the weighted average number of common shares outstanding during the period increased to include, if dilutive, the number of additional common shares that would have been outstanding if the potential common shares had been issued. The Company's potentially dilutive shares include stock options and warrants for common stock.

Because the Company reported a net loss for the three and nine months ended September 30, 2021 and 2020, all potentially dilutive shares of common stock have been excluded from the computation of the dilutive net loss per share for all periods presented. Such potentially dilutive shares of common stock consist of the following:

| | September 30, | |
|---|---|---|
| | **2021** | **2020** |
| **Potentially dilutive securities, excluded:** | | |
| Outstanding stock options | 640,623 | 37,138 |
| Warrants to purchase common stock | 133,401 | 133,401 |
| | 774,024 | 170,539 |

**(3) Fair Value Disclosures**

There were no marketable securities as of September 30, 2021 or December 31, 2020.

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price). Inputs used to measure fair value are classified into the following hierarchy:

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities. The Company's Level 1 assets consist of money market investments. The Company does not have any Level 1 liabilities.
- Level 2—Unadjusted quoted prices in active markets for similar assets or liabilities; unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active; or inputs other than quoted prices that are observable for the asset or liability. The Company does not have any Level 2 assets or liabilities.
- Level 3—Unobservable inputs for the asset or liability. The Company does not have any Level 3 assets or liabilities.

As of September 30, 2021 and December 31, 2020, the Company had $58.2 million and $49.1 million, respectively, of cash equivalents consisting of money market funds with original maturities of 90 days or less. The Company has the ability to liquidate these investments without restriction. The Company determines fair value for these money market funds with Level 1 inputs through quoted market prices. There were no transfers of assets between fair value hierarchy levels during the nine-month period ended September 30, 2021.

***Fair Value of Other Financial Instruments***

The carrying amount of other financial instruments, including accounts payable and a vendor finance agreement, which are included in accounts payable and accrued expenses and other liabilities, approximated fair value due to their short maturities.

**(4) Property and Equipment**

Property and equipment consist of the following (in thousands):

| | Estimated Life | September 30, 2021 | December 31, 2020 |
|---|---|---|---|
| Computer equipment | 3 years | $ 50 | $ 31 |
| Lab equipment | 5 years | 133 | 146 |
| Furniture and fixtures | 5 years | 43 | 38 |
| Computer software | 3 years | 39 | 56 |
| | | 265 | 271 |
| Accumulated depreciation and amortization | | (217) | (250) |
| Property and equipment, net | | $ 48 | $ 21 |

For the nine months ended September 30, 2021 and 2020, depreciation and amortization expense was $11,000 and $6,000, respectively.

**(5) Related Party Arrangements**

*Transactions with the Company's President and Chief Executive Officer*

The Company has entered into unrestricted research grants with its President and Chief Executive Officer's academic research laboratory at the University of Colorado. Funding of any unrestricted research grants is contingent upon the Company's financial condition, and can be deferred or terminated at the Company's discretion. Total expense under these arrangements for the nine months ended September 30, 2021 and 2020 was $331,000 and $248,000 respectively.

**(6) Commitments and Contingencies**

The Company has or is subject to the following commitments and contingencies.

***Employment Agreements***

The Company maintains employment agreements with several key executive employees. The agreements may be terminated at any time by the Company with or without cause upon written notice to the employee, and entitle the employee to wages in lieu of notice for periods not exceeding one calendar year from the date of termination without cause or by the employee for good reason. Certain of these agreements also provide for payments to be made under certain conditions related to a change in control of the Company.

***Operating Leases***

On August 1, 2013 the Company entered into a lease agreement for approximately 5,300 square feet of office facilities in Westminster, Colorado which served as the Company's primary business office from October 1, 2013 until September 30, 2020.

On August 29, 2020 the Company entered into a lease agreement for approximately 5,200 square feet of office facilities in Westminster, Colorado which serves as the Company's primary business office effective October 1, 2020 (October 2020 Lease). The lease term is 42 months beginning October 1, 2020 and includes an option to renew for an additional 36 month term at the then prevailing rental rate. The exercise of the lease renewal option is at the Company's sole discretion. The amounts recorded assume the Company will exercise its renewal option. In June 2021, the Company entered into a sublease agreement for approximately 3,000 square feet of additional office facilities in the Company's primary business office (2021 Lease). The sublease term is 29 months beginning June 2021, with no renewal option. The leases include real estate taxes and insurance, which is not a lease component and is not included in the lease obligation. In addition, common area maintenance charges are based on actual costs incurred and are a non-lease component that is not included in the lease obligation.

Future minimum commitments due under the October 2020 and 2021 Lease agreements as of September 30, 2021 are as follows (in thousands):

| | | |
|---|---|---|
| Remainder of 2021 | $ | 32 |
| 2022 | | 131 |
| 2023 | | 127 |
| 2024 | | 93 |
| 2025 | | 96 |
| Thereafter | | 125 |
| Total remaining lease payments | | 604 |
| Less: imputed lease interest | | (97) |
| Less: Current portion | | (97) |
| Operating lease liability, net of current portion | $ | 410 |

Rent expense, which is included in general and administrative expense, for the nine months ended September 30, 2021 and 2020 was $78,000 and $73,000, respectively.

As of September 30, 2021, the lease liability was $507,000, and the current portion is included in accrued expenses and other liabilities and the non-current portion is in operating lease liability, net of current portion in the accompanying balance sheet. Cash paid for amounts included in the measurement of lease liabilities and the operating cash flows from operating leases for the nine months ended September 30, 2021 and 2020 were $52,000 and $76,000, respectively. The weighted-average remaining lease term for the operating lease as of September 30, 2021 is 5.0 years. The discount rate for the operating lease is 7%.

***Patent Agreement***

In July 2021, the Company entered into a patent assignment agreement (the Agreement) with the University Medical Center of Johannes Gutenberg University Mainz, Germany.

Under the terms of the Agreement, the Company received exclusive world-wide patent rights relating to the use of rNAPc2 as a potential treatment for COVID-19, and other indications, based on the research and discoveries from Univ.-Prof. Dr. Wolfram Ruf, the Scientific Director and Alexander von Humboldt Professor at the Center for Thrombosis and Hemostasis (CTH) of the University Medical Center Mainz, and his collaborators. The Company has upfront and potential milestone obligations to the University Medical Center Mainz that could total approximately €1.6 million and royalty obligations in the low single digit range, if rNAPc2 receives regulatory approval and is commercialized. The term of the Agreement extends to the date of expiration of the last to expire of any of the assigned patents.

**(7)** ***Equity Financings and Warrants***

***Registered Direct Financing***

On June 3, 2020, the Company closed a registered direct offering with certain institutional and accredited investors of 348,000 shares of the Company's common stock, at a purchase price of $9.00 per share, and pre-funded warrants to purchase 325,500 shares of common stock at a purchase price of $8.999 per warrant. All warrants were exercised by the closing date. The net proceeds were approximately $5.3 million, after deducting placement agent fees and other offering expenses. The Company paid JonesTrading a placement agent fee equal to 8.0% of the aggregate gross proceeds and agreed to provide JonesTrading with customary indemnification and contribution rights.

***At the Market Equity Financing***

On January 11, 2017, the Company entered into a Capital on Demand ™ Sales Agreement (the Sales Agreement) with JonesTrading Institutional Services LLC, as agent (JonesTrading), pursuant to which the Company may offer and sell, from time to time through JonesTrading, shares of the Company's common stock, par value $0.001 per share (the Common Stock), having an aggregate offering price of up to $7.3 million. On August 21, 2017, January 25, 2019, March 11, 2019, May 9, 2019, May 20, 2019, June 28, 2019, July 2, 2020 and July 14, 2020, the Company amended its Capital on Demand Sales Agreement. The amendments, among other things, increased the maximum aggregate offering value of shares of the Company's common stock which the Company may issue and sell from time to time under the Sales Agreement from $7.3 million to $32.4 million (the Shares).

Under the amended Sales Agreement, JonesTrading may sell the Shares by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on or through the Nasdaq Capital Market, on any other existing trading market for the Common Stock or to or through a market maker. In addition, under the amended Sales Agreement, JonesTrading may sell the Shares by any other method permitted by law, including in negotiated transactions. The Company may instruct JonesTrading not to sell Shares if the sales cannot be effected at or above the price designated by the Company from time to time.

The Company is not obligated to make any sales of the Shares under the amended Sales Agreement. The offering of Shares pursuant to the amended Sales Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the amended Sales Agreement or (b) the termination of the amended Sales Agreement by JonesTrading or the Company, as permitted therein.

The Company paid JonesTrading a commission rate equal to 3.0% of the aggregate gross proceeds from each sale of Shares and agreed to provide JonesTrading with customary indemnification and contribution rights. The Company will also reimburse JonesTrading for certain specified expenses in connection with entering into and amending the Sales Agreement.

Under the amended Sales Agreement, the Company sold an aggregate of 2,214,301 shares of Common Stock, for net proceeds of approximately $14.4 million, during the year ended December 31, 2020, including initial expenses for executing the “at the market offering” and commissions to the placement agent. This sales agreement terminated in July 2020.

On July 22, 2020, the Company entered into a new Capital on Demand™ Sales Agreement (the 2020 Sales Agreement) with JonesTrading, pursuant to which the Company may offer and sell, from time to time through JonesTrading, shares of the Company’s Common Stock, having an aggregate offering price of up to $54.0 million. During the nine months ended September 30, 2021 and the year ended December 31, 2020, the Company had sold an aggregate of 4,861,993 and 5,066,279 shares of its Common Stock pursuant to the terms of the 2020 Sales Agreement for net proceeds of approximately $23.3 million and $28.9 million, respectively, after deducting expenses for executing the “at the market offering” and commissions paid to the placement agent.

In April 2021, the Company amended the 2020 Sales Agreement and has $50.0 million available for the offering under its prospectus to the Company’s registration statement on Form S-3 (No. 333-254585).

***Warrants***

Warrants to purchase shares of common stock were previously granted as part of various financing and business agreements. All outstanding warrants were recorded in additional paid-in capital at their estimated fair market value at the date of grant using a Black-Scholes option-pricing model.

As of September 30, 2021, these warrants, by year of expiration, are summarized below:

| Year of Expiration | Number of Warrants | Weighted Average Exercise Price |
|---|---|---|
| 2022 | 133,401 | $ 109.80 |

**(8) Share-based Compensation**

For the three and nine month periods ended September 30, 2021 and 2020, the Company recognized the following non-cash, share-based compensation expense in the statements of operations (in thousands):

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2021 | 2020 | 2021 | 2020 |
| Research and development | $ 41 | $ 5 | $ 115 | $ 18 |
| General and administrative | 63 | — | 263 | 7 |
| Total | $ 104 | $ 5 | $ 378 | $ 25 |

Stock option transactions for the nine month period ended September 30, 2021 under the Company’s stock incentive plans were as follows:

| | Number of Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (in years) |
|---|---|---|---|
| Options outstanding at December 31, 2020 | 531,238 | $ 8.71 | 9.68 |
| Granted | 170,200 | 3.51 | |
| Exercised | — | — | |
| Forfeited and cancelled | (60,815) | 12.71 | |
| Options outstanding at September 30, 2021 | 640,623 | $ 6.95 | 9.11 |
| Options exercisable at September 30, 2021 | 125,951 | $ 18.98 | 8.26 |
| Options vested and expected to vest | 639,557 | $ 6.95 | 9.11 |

**(9) Income Taxes**

In accordance with GAAP, a valuation allowance should be provided if it is more likely than not that some or all of the Company's deferred tax assets will not be realized. The Company's ability to realize the benefit of its deferred tax assets will depend on the generation of future taxable income. Due to the uncertainty of future profitable operations and taxable income, the Company has recorded a full valuation allowance against its net deferred tax assets. The Company believes its tax filing positions and deductions related to tax periods subject to examination will be sustained upon audit and, therefore, has no reserve for uncertain tax positions.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*This Management's Discussion and Analysis of Financial Condition and Results of Operations contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the Private Securities Litigation Reform Act of 1995. Examples of these statements include, but are not limited to, statements regarding the following: potential future development plans for rNAPc2 (AB201) and Gencaro, including the potential for rNAPc2 to treat COVID-19, our ability to secure sufficient financing to support our anticipated clinical trials of rNAPc2 and Gencaro, the likelihood that any Phase 3 clinical trial results for Gencaro will satisfy the requirements of our Special Protocol Assessment agreement, the expected features and characteristics of Gencaro, including the potential for genetic variations to predict individual patient response to Gencaro or AB171, Gencaro's potential to treat atrial fibrillation, or AF, future vaccines and treatment options for patients with COVID-19, future treatment options for patients with AF, the potential for Gencaro to be the first genetically-targeted AF prevention treatment, statements regarding potential Phase 3 development plans for Gencaro, including the timing and results thereof, the expected features and characteristics of AB171 as a potential genetically-targeted treatment for peripheral arterial disease, or PAD, and for heart failure, or HF, the potential timeline for development of AB171, including any Investigational New Drug, or IND, application submission related thereto, and the ability of ARCA's financial resources to support its operations through the end of fiscal year 2022, the sufficiency of our current capital to reach certain of our corporate objectives, our ability to obtain additional funding when needed or enter into a strategic or other transaction, including our ability to raise sufficient capital to fund any clinical trials for rNAPc2 and Gencaro and our other operations, the extent to which our issued and pending patents may protect our products and technology, the potential of such product candidates to lead to the development of safe or effective therapies, our ability to enter into collaborations, our ability to maintain listing of our common stock on a national exchange, our future operating expenses, our future losses, our future expenditures, and the sufficiency of our cash resources to maintain operations. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed herein and elsewhere. These and other factors are identified and described in more detail in ARCA's filings with the U.S. Securities and Exchange Commission, or the SEC, including without limitation our annual report on Form 10-K for the year ended December 31, 2020, and subsequent filings. Forward-looking statements may be identified by words including "will," "plan," "anticipate," "believe," "intend," "estimates," "expect," "should," "may," "potential" and similar expressions. We disclaim any intent or obligation to update these forward-looking statements.*

The terms "ARCA," "the Company," "we," "us," "our" and similar terms refer to ARCA biopharma, Inc.

***Overview***

We are a clinical-stage biopharmaceutical company applying a precision medicine approach to the development and commercialization of targeted therapies for cardiovascular diseases. Precision medicine refers to the tailoring of medical treatment to the individual characteristics of patients, using genomic, non-genomic biomarker and other information that extends beyond routine diagnostic categorization. We believe that when implemented correctly precision medicine can enhance therapeutic response, improve patient outcomes, and reduce healthcare costs.

Our lead product candidates are rNAPc2 (AB201) as a potential treatment for COVID-19, the disease syndrome caused by the SARS-CoV-2 virus, and potentially other viral diseases and Gencaro™ (bucindolol hydrochloride) for the treatment of atrial fibrillation, or AF, in patients with chronic heart failure, or HF. rNAPc2 targets COVID-19 patients with biomarker evidence of coagulopathy, while Gencaro is being developed for patients who have a genotype that identifies a drug target associated with heightened efficacy.

***rNAPc2 (AB201) for treatment of COVID-19***

Recombinant Nematode Anticoagulant Protein c2, or rNAPc2 (AB201), is a protein therapeutic in clinical development as a potential treatment for patients with COVID-19. Based on its unique mechanism of action, development history and the clinical evidence from the SARS-CoV-2 pandemic, we believe rNAPc2 has potential to be a beneficial therapy for patients with this serious viral disease. We initiated a Phase 2 clinical trial of rNAPc2 as a potential treatment for patients hospitalized with COVID-19 in the fourth quarter of 2020 and are currently enrolling patients.

Certain patients with severe COVID-19 disease exhibit thrombotic complications and other inflammatory responses suggesting potential dysregulation of the coagulation and immune systems. rNAPc2 is a potent inhibitor of tissue factor, a cellular receptor responsible for initiation of the primary coagulation pathway and appears to be the major activator of the coagulation cascade during viral infection. Tissue factor is also implicated in the immune system inflammatory response to viral infections and in the process of viral dissemination during infection. We believe that evidence from the pandemic implicates tissue factor pathways as an important part of the COVID-19 disease process, and provides a rationale to test rNAPc2 as a potential therapeutic for COVID-19 for its anticoagulant and potential anti-inflammatory properties.

rNAPc2 was originally developed for potential use as an anticoagulant due to its inhibition of the TF-initiated coagulation process. It was evaluated for the prevention of thrombosis in Phase 1 and Phase 2 clinical studies involving over 800 subjects and demonstrated both safety and efficacy in these studies. rNAPc2 has also been investigated as a potential therapeutic for severe viral infections other than COVID-19. Research has shown that viral infections can provoke dysregulated activation of the TF pathway, resulting in abnormal systemic coagulation and related inflammation, leading to potential organ failure and mortality. For this reason, rNAPc2 was tested as a therapeutic in non-human primates, or NHPs, in studies against lethal doses of the Ebola and Marburg viruses, where it showed evidence of efficacy in the form of mortality reduction, decreases in inflammatory biomarkers and, evidence of reduced disseminated intravascular coagulation, a serious condition that causes abnormal blood clotting throughout the body's blood vessels.

SARS-CoV-2 is a new coronavirus identified in late 2019 that belongs to a family of enveloped RNA viruses that include Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS-CoV-1), both of which caused serious human infections of the respiratory system. The disease caused by the SARS-CoV-2 virus has been designated COVID-19. According to the World Health Organization, since this outbreak was first reported in late 2019, there have been over 240 million confirmed cases of COVID-19 and over 4 million deaths worldwide attributed to the virus (as of October 2021).

COVID-19 is associated with a high incidence of both arterial and venous coagulation-related adverse events in large and small blood vessels. These include, stroke, myocardial infarction, or MI, (i.e., heart attack) and pulmonary emboli; as well as, blockage of the smaller peripheral blood vessels in the fingers/toes (COVID-digit). This syndrome is so frequently observed in COVID-19 that it has received the name of COVID-19 Associated Coagulopathy, or CAC. The underlying pathology of CAC is believed to result from thrombo-inflammatory processes triggered by the viral infection. A commonly used biomarker for assessing the presence of abnormal coagulation is a D-dimer test, which is elevated (greater than 0.5) in approximately 40% to 75% of hospitalized COVID-19 patients and is associated with adverse clinical outcomes. Some researchers believe that this and other evidence points to dysregulation of TF pathways in COVID-19 patients that result in the development of thrombotic complications.

As a result of the observed role of coagulation disorders in COVID-19, patients who are hospitalized with the disease are commonly giving anti-coagulant therapy, in particular heparin. We believe that there is a medical need for a COVID-19 therapy that provides anticoagulation therapy and directly inhibits the TF pathway and the inflammatory and viral dissemination processes that may be initiated by TF.

rNAPc2 has shown potential in addressing the coagulation disorder caused by severe viral infections. In preliminary, non-human studies in NHPs against lethal doses of the Ebola and Marburg virus, rNAPc2 lowered D-dimer levels, reduced mortality and exhibited anti-inflammatory effects. We believe more recent research supports our belief that rNAPc2 has the ability to inhibit the activity of TF in multiple processes that contribute to severe viral disease. Taken together, we believe this evidence suggests that rNAPc2 may have therapeutic benefits for patients with serious COVID-19 infections and the accompanying high risk of thrombosis. To our knowledge, rNAPc2 is the only New Molecular Entity anticoagulant, and the only tissue factor inhibitor, currently under evaluation for COVID-19.

As a therapeutic aimed at a host response to a disease syndrome, we believe rNAPc2 potentially could be used in combination with other antiviral drugs. We believe its potential efficacy is not linked to a specific viral genome and may not be diminished by the development of new strains of the SARS-CoV-2 virus through mutation, such as the Delta variant that is now widespread. As a therapeutic addressing a disease, we believe rNAPc2 may have broad spectrum potential against multiple pathogens that have disease elements in common with COVID-19, such as other coronaviruses and other RNA viruses. Therefore, we believe that rNAPc2 has therapeutic potential for future viral outbreaks beyond the current pandemic.

rNAPc2 is a single-chain, 85 amino acid, recombinant protein administered subcutaneously, that has previously been evaluated under three FDA Investigational New Drug, or IND, applications in six Phase 1 and three Phase 2 clinical studies in the United States and Europe. These clinical trials primarily examined the safety, dosing and anticoagulation effects of rNAPc2 in patients with acute coronary syndromes, in patients undergoing knee replacement surgery and in patients undergoing percutaneous coronary interventions. In these trials, involving more than 800 human patients with over 700 exposed to drug, rNAPc2 was generally well-tolerated with a safety profile comparable to commercially available anticoagulants. rNAPc2 is manufactured in an engineered yeast strain by an established methodology following current Good Manufacturing Practices, or cGMP, and we believe this process can be readily scaled to commercial quantities. FDA granted rNAPc2 Orphan Drug Designation status in 2014 for the treatment of viral hemorrhagic fever post-exposure to Ebola virus, but human clinical trials were not conducted.

In October 2020, FDA approved the IND application for rNAPc2 as a potential treatment for patients hospitalized with COVID-19 and it received a Fast-Track designation in November 2020. We initiated the Phase 2b clinical trial of rNAPc2 (AB201), ASPEN-COVID-19, in patients hospitalized with COVID-19 in the fourth quarter of 2020. In July 2021, we increased the ASPEN-COVID-19 clinical trial target enrollment from 100 to 160 patients in an effort to increase the sample size for determining if there are differences in the two rNAPc2 dose regimens being investigated, to decrease variance in the standard of care heparin control arm, in recognition of the study being conducted in different geographic regions and to potentially account for evolving changes in the clinical course of COVID-19. In October 2021, the Data and Safety Monitoring Committee, or DSMC, completed a pre-specified interim analysis and, based on the DSMC’s review of approximately 75% of the projected final efficacy and safety data, recommended completion of the

clinical trial with no modifications to the clinical trial design. We anticipate announcing topline data from this approximately 160 patient international Phase 2b clinical trial in the first quarter of 2022.

We are evaluating rNAPc2 as a treatment for patients hospitalized with COVID-19 who are at high risk for thrombotic complications, as indicated by elevated D-dimer levels. The Phase 2b clinical trial is designed to be a randomized comparison of two-dose regimens of rNAPc2 versus heparin prescribed per local standard of care. The primary endpoint of the clinical trial is the change in D-dimer level from baseline to Day 8 relative to standard of care heparin. If Phase 2b results indicate a favorable effect on D-dimer levels and safety is confirmed, following FDA review of the data and identification of the proposed Phase 3 rNAPc2 dose, we anticipate that clinical investigative sites will begin enrolling patients in a planned Phase 3 clinical trial. The primary endpoint of Phase 3 is planned to be clinical recovery as measured by the Adaptive COVID-19 Treatment Trial ordinal scale, with secondary endpoints that include D-dimer levels and the number of thrombotic events. We believe the Phase 3 clinical trial will be event driven, with an estimated requirement of 450 patients. We believe that favorable results from this Phase 2b/3 clinical trial program could support use of rNAPc2 in COVID-19 patients, given its potential efficacy both as an anticoagulant and an anti-viral agent that we believe counters the dysregulatory immune response and improves clinical recovery.

The clinical trial is being managed in collaboration with the Colorado Prevention Center, or CPC, the University of Colorado's Academic Research Organization with extensive experience in managing vascular and anticoagulation clinical trials.

We have financed the development of rNAPc2 through public equity sales. Our rNAPc2 development plans, including the timeline, depend on our ability to enroll patients during the COVID-19 pandemic, the results of our Phase 2b clinical trial, FDA guidance, and availability of drug product, all of which are currently uncertain.

We own the clinical development program of rNAPc2, including the Phase 2 clinical development. If rNAPc2 is successfully developed, we believe it will have intellectual property protection, including 12 years of market exclusivity as an innovative biologic product under FDA law in the United States, 10 years data protection exclusivity in the European Union, or EU, and potentially patent protection in addition to this. We have filed an international patent application for the use of rNAPc2 in COVID-19 and plan to prosecute this patent in the United States and other markets. If this patent issues in the United States, we believe it could provide intellectual property protection into approximately 2040. We plan to pursue strategic co-development and partnering opportunities for rNAPc2 development and commercialization.

In July 2021, we entered into a patent assignment agreement, or the Agreement, with the University Medical Center of Johannes Gutenberg University Mainz, Germany. Under the terms of the Agreement, we received exclusive world-wide patent rights relating to the use of rNAPc2 as a potential treatment for COVID-19, and other indications, based on the research and discoveries from Univ.-Prof. Dr. Wolfram Ruf, the Scientific Director and Alexander von Humboldt Professor at the Center for Thrombosis and Hemostasis (CTH) of the University Medical Center Mainz, and his collaborators. We have upfront and potential milestone obligations to the University Medical Center Mainz that could total approximately €1.6 million and royalty obligations in the low single digit range, if rNAPc2 receives regulatory approval and is commercialized. The term of the Agreement extends to the date of expiration of the last to expire of any of the assigned patents.

***Gencaro™ (bucindolol hydrochloride) for Atrial Fibrillation***

Gencaro™ (bucindolol hydrochloride) is a pharmacogenetically-targeted beta-adrenergic receptor antagonist with mild vasodilator properties that we are developing for the treatment of atrial fibrillation in patients with heart failure. We believe the pharmacology of Gencaro is unique and its efficacy can be enhanced by prescribing it to patients with a common genotypic variant that is present in approximately 50% of the North American and European general populations. This gene can be detected with a simple genetic test.

We are developing Gencaro to treat atrial fibrillation, or AF, in patients with chronic heart failure, or HF. AF is the most common form of cardiac arrhythmia, a disruption of the heart’s normal rhythm or rate. HF is a chronic condition in which the heart is unable to pump enough blood to meet the body’s needs. AF and HF commonly occur together. In HF patients, the development of AF leads to worsening symptoms, and increased risk of hospitalization and death. Current treatment options for AF in HF patients are limited, and can be invasive, costly and dangerous.

Our development plan for Gencaro focuses on the treatment of AF in patients with higher ejection fraction HF, those who have an ejection fraction, or EF, of 40% and higher who also have the genotype we believe is optimal for Gencaro efficacy. This population of HF encompasses more than half of all HF patients in the United States and Europe. There are currently few approved or effective drug therapies to treat AF or HF in this patient population.

Our development plan for Gencaro is based on our recently published analysis of the Phase 2b clinical trial of Gencaro for the prevention of AF in HF patients, known as GENETIC-AF. This analysis showed novel results for Gencaro in patients in the clinical trial with EF’s of 40% and higher. The Phase 3 pivotal clinical trial of Gencaro conducted under an SPA will include secondary endpoints that are intended to capture some of this new information, such as a reduction in the need to deploy rhythm control interventions including electrical cardioversion, catheter ablation and use of anti-arrhythmic drugs and avoidance of drug-related

complications such as bradycardia. Based on these analyses, we were issued a United States patent in February 2021 for the use of Gencaro in this patient population. We believe this patent will substantially extend the patent protection for our planned development of Gencaro into 2039. We are seeking similar patent protection in other countries.

We currently have an agreement with the FDA, known as a Special Protocol Assessment, or SPA, for the requirements of a Gencaro Phase 3 clinical trial that would support approval of Gencaro if successful.

We believe that patients with HF and AF represent a major unmet medical need, and this need is most pronounced in patients with EF values of 40% and above. This EF range constitutes more than half of all chronic HF in the United States and Europe, as well as in Japan and China, and there are currently few approved, effective or guideline-recommended therapies for these patients to treat either their AF or HF. AF is a very common complication in these patients, with estimates of AF incidence ranging from 40% to 60%. Beta-blockers approved for HF are commonly used off-label to control heart rate in these patients, but they are not considered effective in preventing AF and none are approved for patients with EF ≥ 40%. Other anti-arrhythmic drugs approved for the treatment of AF have adverse side effects and in HF patients are either contraindicated or have label warnings for use due to an increased risk of mortality. Interventional procedures for AF, such as catheter ablation and electrical cardioversion, are invasive, expensive, and often temporary; these interventions also typically require the continued use of beta blockers and other anti-arrhythmic drugs post-intervention.

We believe that Gencaro, if approved, may be a safe and more effective therapy for the treatment of higher ejection fraction HF patients with AF. We believe there are several potentially important attributes that would differentiate Gencaro from existing therapies, including:

- More effective rhythm control compared to the current standard of care;
- Reduction in the need for catheter ablation, electrical cardioversion, or toxic anti-arrhythmic drugs;
- Maintenance of rhythm control after a successful AF catheter ablation;
- Effective rate control with lower risk of treatment-limiting, adverse event producing bradycardia;
- Reduction in symptoms and improvement in quality of life;
- Reduced health care burden;
- Foundational beta-blocker benefits for HF and unique evidence of efficacy in HF patients with AF;
- One of the only drug therapies approved and shown effective for AF in HF patients with EF ≥ 40%, and the only one in its drug class.

We have an international patent portfolio for Gencaro in the United States, the EU, and other major markets, as well as new chemical entity status, including a new patent that we believe will give us a strong intellectual property position to at least approximately 2039 in the United States; we have filed applications similar to this new patent in international territories. We have developed a laboratory platform for the diagnostic test that would be used to prescribe Gencaro; this platform was approved by FDA for use in the Phase 2B clinical trial. We retain all rights to this test platform; we expect to use it in future clinical trials, and we believe it could be one of multiple diagnostic platforms used for commercialization.

To support the continued development of rNAPc2 and Gencaro, we will need additional financing to fully fund the planned clinical trials, and our general and administrative costs through the clinical trials' projected completion and potential commercialization. Considering the substantial time and costs associated with the development of rNAPc2 and Gencaro and the risk that we may be unable to raise a significant amount of capital on acceptable terms, we are also pursuing co-development and commercialization partnering opportunities with large pharmaceutical and/or specialty pharmaceutical companies and may pursue a strategic combination or other strategic transactions. If we are unable to obtain sufficient financing or are unable to complete a strategic transaction, we may discontinue our development activities on rNAPc2 or Gencaro or discontinue our operations.

We believe our cash and cash equivalents as of September 30, 2021 will be sufficient to fund our operations through the end of fiscal year 2022, including the projected costs for the rNAPc2 (AB201) Phase 2b clinical trial. Conducting a Phase 3 rNAPc2 clinical trial or the Phase 3 PRECISION-AF trial would likely require additional financing. However, changing circumstances may cause us to consume capital significantly faster or slower than currently anticipated. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate; therefore, we may have to raise additional capital for other clinical trials of rNAPc2. Initiating any Phase 3 clinical trial of Gencaro is dependent on sustained improvement in the COVID-19 pandemic and will require additional financing.

In 2017, we entered into a sales agreement with a placement agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in an “at the market offering.” In 2020, we further amended the sales agreement to increase the maximum aggregate value of shares which we may issue and sell from time to time under this sales agreement to $32.4 million. This sales agreement terminated in July 2020. Under this sales agreement, we had sold an aggregate of 3,302,159 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $32.3 million. Net proceeds received in this offering were approximately $30.8 million, after deducting expenses for executing the “at the market offering” and commissions paid to the placement agent.

In July 2020, we entered into a new sales agreement with a placement agent to sell, from time to time, our common stock having an aggregate offering price of up to $54.0 million, in an “at the market offering.” As of February 2021, we had sold an aggregate of 9,928,272 shares of our common stock pursuant to the terms of such sales agreement for aggregate gross proceeds of approximately $54.0 million. Net proceeds received in this offering were approximately $52.2 million, after deducting expenses for executing the “at the market offering” and commissions paid to the placement agent.

In April 2021, we amended the new sales agreement and have $50.0 million available for the offering under our prospectus to our registration statement on Form S-3 (No. 333-254585).

In March 2020, the World Health Organization declared the outbreak of COVID-19, a novel strain of Coronavirus, a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads. We do not expect a material financial effect as a result of the pandemic. However, if the pandemic continues to be a severe worldwide crisis, it could have a material adverse effect on our business, results of operations, financial condition and cash flows.

***Results of Operations***

***Research and Development Expenses***

Research and development, or R&D, expense is comprised primarily of personnel costs, clinical development, manufacturing process development, and regulatory activities and costs. Our R&D expense is almost entirely generated by our activities relating to the development of rNAPc2 (AB201).

R&D expense for the three months ended September 30, 2021 was $3.4 million compared to $1.1 million for the corresponding period of 2020, an increase of $2.4 million. R&D expense for the nine months ended September 30, 2021 was $9.9 million compared to $1.8 million for the corresponding period of 2020, an increase of approximately $8.1 million.

Clinical expense increased approximately $1.7 million and $5.0 million for the three and nine months ended September 30, 2021, as compared to the corresponding periods of 2020. Manufacturing process development costs increased approximately $0.3 million and $2.0 million for the three and nine months ended September 30, 2021, as compared to the corresponding periods of 2020. The increase was related to the initiation of our rNAPc2 (AB201) clinical trial in the second half of 2020. The remaining increase is primarily a result of higher outside services and consulting costs.

R&D personnel costs increased approximately $0.3 million and $0.7 million for the three and nine months ended September 30, 2021, as compared to the corresponding periods of 2020.

R&D expense in 2021 is expected to be higher than 2020, as we continue our rNAPc2 (AB201) international Phase 2b clinical trial.

***General and Administrative Expenses***

General and administrative, or G&A, expenses primarily consist of personnel costs, consulting and professional fees, insurance, facilities and depreciation expenses, and various other administrative costs.

G&A expenses were $1.3 million for the three months ended September 30, 2021 compared to $0.9 million for the corresponding period of 2020, an increase of $0.3 million. G&A expenses were $3.8 million for the nine months ended September 30, 2021 compared to $2.9 million for the corresponding period of 2020, an increase of $0.9 million The increases were primarily a result of higher personnel and insurance costs in 2021.

G&A expenses in the last quarter of 2021 are expected to be consistent with the third quarter of 2021 as we maintain administrative activities to support our ongoing operations.

***Interest and Other Income***

Interest and other income was $4,000 and $1,000 in the three months ended September 30, 2021 and 2020, respectively. Interest and other income was $9,000 and $27,000 in the three months ended September 30, 2021 and 2020, respectively.

Interest income for the remainder of 2021 is expected to be negligible.

***Interest Expense***

Interest expense was $2,000 and $9,000 for the three and nine months ended September 30, 2020. Based on our current capital structure, interest expense for the remainder of 2021 is expected to be negligible.

***Liquidity and Capital Resources***

*Cash and Cash Equivalents*

| | September 30, 2021 | December 31, 2020 |
|---|---|---|
| | (in thousands) | |
| Cash and cash equivalents | $ 58,313 | $ 49,071 |

As of September 30, 2021, we had total cash and cash equivalents of $58.3 million, as compared to $49.1 million as of December 31, 2020. The net increase of $9.2 million primarily reflects the net proceeds of $23.1 million from the issuance of common stock, offset by $13.8 million of cash used in operating activities during the nine months ended September 30, 2021.

***Cash Flows from Operating, Investing and Financing Activities***

| | Nine Months Ended September 30, | |
|---|---|---|
| | 2021 | 2020 |
| | (in thousands) | |
| Net cash (used in) provided by: | | |
| Operating activities | $ (13,815) | $ (4,730) |
| Investing activities | (36) | (6) |
| Financing activities | 23,093 | 47,468 |
| Net increase in cash and cash equivalents | $ 9,242 | $ 42,732 |

Net cash used in operating activities for the nine months ended September 30, 2021 increased $9.1 million compared with the same period in 2020. This was primarily due to higher outflows related to changes in operating assets and liabilities and a higher net loss in 2021, as discussed in Results of Operations above.

Net cash used in investing activities for the nine months ended September 30, 2021 was $36,000 for the purchase of property and equipment. Net cash used in investing activities for the nine months ended September 30, 2020 was $6,000 for the purchase of property and equipment.

Net cash provided by financing activities was $23.1 million for the nine months ended September 30, 2021 related to net proceeds from sales of our common stock in our “at the market” equity offering in the period. Net cash provided by financing activities was $47.5 million for the nine months ended September 30, 2020 representing $47.7 million in net proceeds from sales of our common stock in our registered direct equity offering and our “at the market” equity offering in the period, less $0.3 million of payments on a vendor finance arrangement.

***Sources and Uses of Capital***

Our primary sources of liquidity to date have been capital raised from issuances of shares of our preferred and common stock. The primary uses of our capital resources to date have been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments, and spending on capital items.

In July 2020, we entered into a new sales agreement with a placement agent to sell, from time to time, our common stock having an aggregate offering price of up to $54.0 million, in an “at the market offering.” As of February 2021, we had sold an aggregate of 9,928,272 shares of our common stock pursuant to the terms of such sales agreement for aggregate gross proceeds of approximately $54.0 million. Net proceeds received in this offering were approximately $52.2 million, after deducting expenses for executing the “at the market offering” and commissions paid to the placement agent.

In April 2021, we amended the new sales agreement and have $50.0 million available for the offering under our prospectus to our registration statement on Form S-3 (No. 333-254585).

In March 2020, the World Health Organization declared the outbreak of COVID-19, a novel strain of Coronavirus, a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads. We do not expect a material financial effect as a result of the pandemic. However, if the pandemic continues to be a severe worldwide crisis, it could have a material adverse effect on our business, results of operations, financial condition and cash flows.

Our ability to execute our development programs in accordance with our projected time line depends on a number of factors, including, but not limited to, the following:

- the costs and timing for the potential additional clinical trials in order to gain possible regulatory approval for rNAPc2, Gencaro or any other product candidate;
- the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;
- our ability to retain the listing of our common stock on the Nasdaq Capital Market;
- our ability to control costs associated with its operations;
- general economic and industry conditions affecting the availability and cost of capital, including as a result of the COVID-19 pandemic;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the terms and conditions of our existing collaborative and licensing agreements.

We believe our cash and cash equivalents balance as of September 30, 2021 will be sufficient to fund our operations through the end of fiscal year 2022. Conducting a Phase 3 rNAPc2 clinical trial or the Phase 3 PRECISION-AF trial would likely require additional financing. However, changing circumstances may cause us to consume capital significantly faster or slower than currently anticipated. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate; therefore, we may have to raise additional capital for clinical trials of rNAPc2. Initiating any Phase 3 clinical trial of Gencaro is dependent on our obtaining additional financing. We may not be able to raise sufficient capital on acceptable terms, or at all, to continue development and potential commercialization of rNAPc2 or Gencaro or to otherwise continue operations and may not be able to execute any strategic transaction.

***Critical Accounting Policies and Estimates***

A critical accounting policy is one that is both important to the portrayal of our financial condition and results of operation and requires our management’s most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. Our significant accounting policies are described in Note 1 of “Notes to Financial Statements” included within our 2020 Annual Report on Form 10-K filed with the SEC. Following is a discussion of the accounting policies that we believe involve the most difficult, subjective or complex judgments and estimates.

*Accrued Outsourcing Expenses*

As part of the process of preparing our financial statements, we are required to estimate accrued outsourcing expenses. This process involves identifying services that third parties have performed on our behalf and estimating the level of service performed and the associated cost incurred for these services as of the balance sheet date. Examples of estimated accrued outsourcing expenses include contract service fees, such as fees payable to contract manufacturers in connection with the production of materials related to our drug product, and service fees from clinical research organizations. We develop estimates of liabilities using our judgment based upon the facts and circumstances known at the time.

***Off-Balance Sheet Arrangements***

We have not participated in any transactions with unconsolidated entities, such as special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements.

***Indemnifications***

In the ordinary course of business, we enter into contractual arrangements under which we may agree to indemnify certain parties from any losses incurred relating to the services they perform on our behalf or for losses arising from certain events as defined within the particular contract. Such indemnification obligations may not be subject to maximum loss clauses. We have entered into indemnity agreements with each of our directors, officers and certain employees. Such indemnity agreements contain provisions, which are in some respects broader than the specific indemnification provisions contained in Delaware law. We also maintain an insurance policy for our directors and executive officers insuring against certain liabilities arising in their capacities as such.

## ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

## ITEM 4. CONTROLS AND PROCEDURES

***Evaluation of Disclosure Controls and Procedures***

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) of the Securities Exchange Act of 1934, an evaluation was carried out under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) as of the end of the quarter covered by this report. Based on the foregoing, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at a reasonable level of assurance.

***Changes in Internal Control over Financial Reporting***

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that would materially affect or is reasonably likely to materially affect, our internal control over financial reporting.

## PART II. OTHER INFORMATION

### ITEM 1. LEGAL PROCEEDINGS

None

### Item 1A. Risk Factors

*An investment in our securities involves certain risks, including those set forth below and elsewhere in this report. In addition to the risks set forth below and elsewhere in this report, other risks and uncertainties not known to us, that are beyond our control or that we deem to be immaterial may also materially adversely affect our business operations. You should carefully consider the risks described below as well as other information and data included in this report.*

**Summary of Risk Factors**

**Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Form 10-Q and our other filings with the SEC, before making an investment decision regarding our common stock.**

- if we are not able to successfully develop, obtain FDA approval for, and provide for the commercialization of rNAPc2 or Gencaro in a timely manner, we may not be able to continue our business operations;
- if we encounter difficulties enrolling patients in our clinical trials, any potential enrollment milestones or potential regulatory approvals could be delayed or otherwise adversely affected;
- our clinical trials for our product candidates may not yield results that will enable us to further develop our products and obtain regulatory approvals necessary to sell them;
- we may not achieve our projected development goals in the time frames we announce and expect;
- we expect the PRECISION-AF clinical trial will require substantially more capital to complete, and we cannot guarantee when or if we will be able to secure such additional financing;
- we will need to raise substantial additional funds through public or private equity or debt transactions and/or complete one or more strategic transactions, to continue development of rNAPc2, Gencaro or any of our other product candidates. If we are unable to raise such financing or complete such a transaction, we may not be able to continue operations;
- if we are not able to maintain the requirements for listing on the Nasdaq Capital Market, we could be delisted, which could have a material adverse effect on our ability to raise additional funds as well as the price and liquidity of our common stock;
- our business could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 global pandemic, in regions where we or third parties on which we rely may have clinical trial sites or other business operations.
- we depend or may depend on third parties to conduct clinical trials and provide diagnostic information, as well as to develop, commercialize and/or manufacture our product candidates;
- unless we are able to generate sufficient product revenue, we will continue to incur losses from operations and will not achieve or maintain profitability. We are years away from commercializing a product and generating product revenue;
- our product candidates are subject to extensive regulation, which can be costly and time-consuming, and unsuccessful or delayed regulatory approvals could increase our future development costs or impair our future revenue;
- if our product candidates receive regulatory approval, we would be subject to ongoing regulatory obligations and restrictions, which may result in significant expenses and limit our ability to develop and commercialize other potential products;
- transitioning from a clinical development stage company will require successful completion of a number of steps, many of which are outside of our control and, consequently, we can provide no assurance of our successful and timely transition from a clinical development stage company;
- if approved by the FDA, rNAPc2 or Gencaro will be entering a competitive marketplace and may not succeed;

- if we fail to identify and license or acquire other products or product candidates, then we may be unable to expand our business, and the acquisition or licensing of other products or product candidates may put a strain on our operations and will likely require us to seek additional financing;
- the loss of any rights to market key products would significantly impair our operating results;
- third parties may own or control patents or patent applications that we may be required to license to commercialize our product candidates or that could result in litigation that would be costly and time consuming;
- our intellectual property rights may not preclude competitors from developing competing products and our business may suffer.

**Risks Related to Our Business and Financial Condition**

***If we are not able to successfully develop, obtain FDA approval for, and provide for the commercialization of rNAPc2 or Gencaro in a timely manner, we may not be able to continue our business operations.***

We currently have no products that have received regulatory approval for commercial sale. The process to develop, obtain regulatory approval for and commercialize potential product candidates is long, complex and costly.

Failure to demonstrate that a product candidate, including rNAPc2 or Gencaro, is safe and effective, or significant delays in demonstrating such safety and efficacy, would adversely affect our business. Failure to obtain marketing approval of rNAPc2 or Gencaro from appropriate regulatory authorities, or significant delays in obtaining such approval, would also adversely affect our business and could, among other things, preclude us from completing a strategic transaction or obtaining additional financing necessary to continue as a going concern.

Even if approved for sale, a product candidate must be successfully commercialized to generate value. We do not currently have the capital resources or management expertise to commercialize rNAPc2, Gencaro or any of our other product candidates and, as a result, will need to complete a strategic transaction, or, alternatively, raise substantial additional funds to enable commercialization of rNAPc2, Gencaro or any of our other product candidates, if approved. Failure to successfully provide for the commercialization of rNAPc2, Gencaro or any other product candidate, if approved, would damage our business.

***If we encounter difficulties enrolling patients in our clinical trial of rNAPc2, any potential enrollment milestones or potential regulatory approvals could be delayed or otherwise adversely affected.***

We may encounter difficulty enrolling a sufficient number of patients in the trial, due to circumstances which are outside our control, including improvements in the COVID-19 pandemic resulting from the development of vaccines and therapies, as well as other clinical trials or capacity constraints at potential COVID-19 clinical trial sites, that may limit the availability of study participants. As a result, we may need to delay or terminate our trial, which would have a negative impact on our business. Delays in enrolling patients in the clinical trial of rNAPc2 would also adversely affect our ability to meet projected enrollment milestones or timelines for completing the study and obtaining regulatory approval. Development of other COVID-19 targeted therapies may mean there are no patients who need rNAPc2 as a therapy.

***rNAPc2 may not yield results that will enable us to further develop it as a therapy and obtain regulatory approvals necessary to be used as a drug.***

We will receive regulatory approval for our product candidates only if we can demonstrate, in carefully designed and conducted clinical trials, that the product candidate is safe and effective. We do not know whether any future clinical trials for rNAPc2, Gencaro or any other product candidate will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products. rNAPc2 has never been tested for safety or efficacy in any pre-clinical COVID-19 models or any patients diagnosed with COVID-19. It may not be effective for any COVID-19 associated diseases.

The results from preclinical testing and early clinical trials may not be predictive of results from later studies, including our studies of rNAPc2. We may suffer significant setbacks in advanced clinical trials, even after seeing promising results in earlier studies. Based on results at any stage of clinical trials, we may decide to repeat or redesign a trial or discontinue development of one or more of our product candidates, including rNAPc2. If we fail to adequately demonstrate the safety and efficacy of our rNAPc2, or other product candidates, we will not be able to obtain the required regulatory approvals to commercialize it and our business, results of operations and financial condition would be materially adversely affected.

In addition, administering rNAPc2, or other product candidates, to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of rNAPc2, or other product candidates, and could result in the FDA or other regulatory authorities denying approval of rNAPc2, or other product candidates, for any or all targeted indications.

***We may not achieve our projected development goals in the time frames we announce and expect.***

We set goals for, and make public statements regarding, the timing of certain accomplishments, such as the initiation of our clinical trials, including rNAPc2, the duration of the planned rNAPc2 Phase 2b clinical trial, the steps for commencing and continuing our clinical trials, the disclosure of trial results, the obtainment of regulatory approval and the sale of drug products, which we sometimes refer to as milestones. These milestones may not be achieved, and the actual timing of these events can vary dramatically due to a number of factors such as delays or failures in our clinical trials, disagreements with any collaborative partners, the uncertainties inherent in the regulatory approval process and manufacturing scale-up, delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products or our inability to obtain sufficient financing in a timely manner. There can be no assurance that we will make regulatory submissions or receive regulatory approvals as planned. If we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected.

***We expect the PRECISION-AF clinical trial will require substantially more capital to complete, and we cannot guarantee when or if we will be able to secure such additional financing.***

We have put the potential initiation of the PRECISION-AF trial on hold due to the ongoing COVID-19 pandemic and prioritizing the development of rNAPc2. Initiation of the PRECISION-AF clinical trial will depend on receiving additional funding and an abatement of the COVID-19 pandemic to the point of being able to recruit patients for a cardiovascular clinical trial. We will need to secure additional financing in order to initiate enrollment of our Phase 3 PRECISION-AF clinical trial. Even if we can begin enrolling patients, we expect to have to raise significant additional capital to continue enrollment. If we are not able to obtain financing in the future or on acceptable terms, we may have to terminate the clinical trial early, which could adversely affect our business.

***We will need to raise substantial additional funds through public or private equity or debt transactions and/or complete one or more strategic transactions, to continue development of rNAPc2, Gencaro or any of our other product candidates. If we are unable to raise such financing or complete such a transaction, we may not be able to continue operations.***

As a result of the expected development timeline to potentially obtain FDA approval for rNAPc2 or Gencaro, if at all, the substantial additional costs associated with the development of our product candidates, including the costs associated with clinical trials related thereto, and the substantial cost of commercializing rNAPc2 or Gencaro, if approved, we will need to raise substantial additional funding through public or private equity or debt transactions or a strategic combination or partnership. If we are delayed in obtaining funding or are unable to complete a strategic transaction, we may discontinue our development activities on rNAPc2, Gencaro and our other product candidates or discontinue our operations. Even if we are able to fund continued development of rNAPc2, Gencaro or any of our other product candidates is approved, we expect that we will need to complete a strategic transaction or raise substantial additional funding through public or private equity or debt securities to successfully commercialize rNAPc2, Gencaro or any other product candidate.

We believe our cash and cash equivalents as of September 30, 2021 will be sufficient to fund our operations through the end of fiscal year 2022. Conducting a Phase 3 rNAPc2 clinical trial or the Phase 3 PRECISION-AF trial would likely require additional financing. On July 22, 2020, we entered into a new sales agreement with a placement agent to sell, from time to time, our common stock having an aggregate offering price of up to $54.0 million, in an “at the market offering.” As of September 30, 2021, we sold an aggregate of 9,928,272 shares of our common stock pursuant to the terms of such sales agreement for aggregate gross proceeds of approximately $54.0 million. Net proceeds received in this offering were approximately $52.2 million, after deducting expenses for executing the “at the market offering” and commissions paid to the placement agent. In April 2021, we amended the new sales agreement and have $50.0 million available for the offering under our prospectus to our registration statement on Form S-3 (No. 333-254585). Sales of our common stock dilute the ownership interest of our stockholders and may cause the price per share of our common stock to decrease. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate.

Additionally, in March 2020, the World Health Organization declared the outbreak of COVID-19 a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads. The economic uncertainty surrounding the COVID-19 pandemic may dramatically reduce our ability to secure equity or debt financing necessary to support our operations. We are unable to currently estimate the financial effect of the pandemic. If the pandemic continues to be a severe worldwide crisis, economic conditions may cause capital not to be available to us, or not be available on acceptable terms, regardless of our business efforts. We have put the potential initiation of the PRECISION-AF clinical trial on hold due to the ongoing COVID-19 pandemic and prioritizing the development of rNAPc2. Initiation of the PRECISION-AF clinical trial will depend on receiving additional funding and an abatement of the COVID-19 pandemic to the point of being able to recruit patients for a cardiovascular clinical trial.

Our liquidity, and our ability to raise additional capital or complete any strategic transaction, depends on a number of factors, including, but not limited to, the following:

- the costs and timing for potential additional clinical trials in order to gain possible regulatory approval for rNAPc2, Gencaro and our other product candidates;
- the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;
- our ability to retain the listing of our common stock on the Nasdaq Capital Market;
- general economic and industry conditions affecting the availability and cost of capital, including as a result of the COVID-19 pandemic;
- our ability to control costs associated with our operations;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the terms and conditions of our existing collaborative and licensing agreements.

The sale of additional equity or convertible debt securities would likely result in substantial dilution to our stockholders. If we raise additional funds through the incurrence of indebtedness, the obligations related to such indebtedness would be senior to rights of holders of our capital stock and could contain covenants that would restrict our operations. We also cannot predict what consideration might be available, if any, to us or our stockholders, in connection with any strategic transaction. Should strategic alternatives or additional capital not be available to us, or not be available on acceptable terms, we may be unable to realize value from our assets and discharge our liabilities in the normal course of business which may, among other alternatives, cause us to further delay, substantially reduce or discontinue operational activities to conserve our cash resources.

***We have received an SPA agreement from the FDA relating to our planned Phase 3 program for Gencaro. This SPA agreement does not guarantee approval of Gencaro or any other particular outcome from regulatory review.***

In 2019, we received an SPA agreement from the FDA for our planned Phase 3 clinical trial of Gencaro. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of certain clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to the effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in a SPA letter or the minutes of a meeting between the sponsor and the FDA.

However, an SPA agreement does not guarantee approval of a product candidate, even if the trial is conducted in accordance with the protocol. Moreover, the FDA may revoke or alter our SPA agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, we fail to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by us in our request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Even though we obtained an agreement on our SPA, we cannot assure you that our planned Phase 3 clinical trial will succeed, will be deemed binding by the FDA under our SPA agreement, or will result in any FDA approval for Gencaro. We may also alter the design of the trial to focus on endpoints that are not covered by the SPA. Moreover, if the FDA revokes or alters its agreement under our SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval, which could materially adversely affect our business, financial condition and results of operations.

***If we are not able to maintain the requirements for listing on the Nasdaq Capital Market, we could be delisted, which could have a material adverse effect on our ability to raise additional funds as well as the price and liquidity of our common stock.***

Our common stock is currently listed on the Nasdaq Capital Market. To maintain the listing of our common stock on the Nasdaq Capital Market we are required to meet certain listing requirements, including, among others, (i) a minimum closing bid price of $1.00 per share, (ii) a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least $1 million and (iii) either: (x) stockholders' equity of at least $2.5 million; or (y) a total market value of listed securities of at least $35 million.

We have received three potential delisting notices from Nasdaq since 2012. In each of 2012, 2015 and 2018, we received notification from Nasdaq of potential delisting of our shares from the Nasdaq Capital Market because the closing bid price of our common stock had not met the minimum closing bid price of $1.00 per share during the preceding 30 business days. We subsequently regained compliance with Nasdaq's minimum closing bid price requirements related to the 2012, 2015 and 2018 notices, by effecting a 1-for-6 reverse split of our common stock in March 2013, a 1-for-7 reverse split of our common stock in September 2015 and a 1-for-18 reverse split of our common stock in April 2019. Despite effecting a 1-for-18 reverse split of our common stock in April 2019, there can be no assurance that the market price per share of our common stock will remain in excess of the $1.00 minimum bid price for a sustained period of time. The continuing effect of our reverse stock split on the market price of our common stock cannot be predicted with any certainty, and the history of similar stock split combinations for companies in like circumstances is varied. It is possible that the per share price of our common stock after the reverse stock split will not rise in proportion to the reduction in the number of shares of common stock outstanding resulting from the reverse stock split, effectively reducing our market capitalization, and there can be no assurance that the market price per post-reverse split share will either exceed or remain in excess of the $1.00 minimum bid price for a sustained period of time. The market price of our common stock may vary based on other factors that are unrelated to the number of shares outstanding, including our future performance.

The delisting of our common stock from a national exchange could impair the liquidity and market price of the common stock. It could also materially, adversely affect our access to the capital markets, and any limitation on market liquidity or reduction in the price of the common stock as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all.

In future periods, if we do not meet the minimum stockholders' equity, minimum closing bid price requirements, or any other listing requirements, we would be subject to delisting from the Nasdaq Capital Market.

As of November 1, 2021, the closing price of our common stock was $2.70 per share, and the total market value of our listed securities was approximately $38.9 million. As of September 30, 2021, we had stockholders' equity of $56.6 million.

***Our financial statements for the quarter ended September 30, 2021 were prepared assuming that we will continue as a going concern. Our management has concluded that due to our need for additional capital, and the uncertainties surrounding our ability to raise such funding, there may be uncertainty about our ability to continue as a going concern in future years.***

Our financial statements for the quarter ended September 30, 2021 were prepared assuming that we will continue as a going concern. The going concern basis of presentation assumes that we will continue in operation for the foreseeable future and will be able to realize our assets and discharge our liabilities and commitments in the normal course of business and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from our inability to continue as a going concern. As of December 31, 2019, our management and our independent registered public accounting firm concluded that, due to our need for additional capital and the uncertainties surrounding our ability to raise such funding, substantial doubt existed as to our ability to continue as a going concern for a period from one year after our annual financial statements had been issued. We believe our cash and cash equivalents as of September 30, 2021 will be sufficient to fund our operations through the end of fiscal year 2022. Conducting a Phase 3 rNAPc2 clinical trial or the Phase 3 PRECISION-AF trial would likely require additional financing. We cannot be certain that we will be able to make any other sale of our common stock in any future offering to cover our future capital needs, or at all. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. If we are delayed in completing or are unable to complete additional funding and/or a strategic transaction, we may discontinue our development activities or operations, but there are no assurances that these reductions would be sufficient to allow us to continue to operate as a going concern. Therefore, even if we resolve this uncertainty, our independent registered public accountants and/or management could conclude that uncertainty as to our ability to continue as a going concern could exist at a future date.

We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate. We may be forced to reduce our operating expenses and raise additional funds to meet our working capital needs, principally through the additional sales of our securities or debt financings. However, we cannot guarantee that we will be able to obtain sufficient additional funds when needed or that such funds, if available, will be obtainable on terms satisfactory to us. If we are unable to raise sufficient additional capital or complete a strategic transaction, we may be unable to continue to fund our operations, develop rNAPc2, Gencaro or our other product candidates, or realize value from our assets and discharge our liabilities in the normal course of business. If we cannot raise sufficient funds, we may have to liquidate our assets, and might realize significantly less than the values at which they are carried on our financial statements, and stockholders may lose all or part of their investment in our securities.

***Our business could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 global pandemic, in regions where we or third parties on which we rely may have clinical trial sites or other business operations. We anticipate having clinical trial sites in countries that have been directly affected by COVID-19 and depend on third party manufacturing operations for various stages of our supply chain.***

Our business could be adversely affected by health epidemics, including the ongoing COVID-19 pandemic, in regions where we may have concentrations of future clinical trial sites or other business operations.

If the recent COVID-19 outbreak continues to spread, we may need to further limit operations or implement limitations, including work-from-home policies. There is a risk that other countries or regions may be less effective at containing COVID-19, or it may be more difficult to contain if the outbreak reaches a larger population or broader geography, in which case the risks described herein could be elevated significantly.

In addition, third party manufacturing of our drug product candidates and suppliers of the materials used in the production of our drug product candidates may be impacted by significant delays or restrictions resulting from the COVID-19 outbreak which may disrupt our supply chain or limit our ability to manufacture drug product candidates for our clinical trials.

The ultimate impact of the COVID-19 outbreak or a similar future health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

***If we encounter difficulties enrolling patients in any future clinical trials, our future trials could be delayed or otherwise adversely affected.***

If we have difficulty enrolling a sufficient number of patients in any future clinical trial, we may need to delay or terminate our trial, which would have a negative impact on our business. Delays in enrolling patients in any future clinical trials would also adversely affect our ability to generate any product, milestone and royalty revenues under collaboration agreements, if any, and could impose significant additional costs on us or on any future collaborators.

Development beyond our control may impact our ability to enroll patients in an rNAPc2 (AB201) Phase 2b clinical trial, such as the development of vaccines for the SARS-CoV-2 virus or the development of other therapies for COVID-19 disease.

The GENETIC-AF clinical trial required that we identify and enroll a large number of patients with the condition under investigation and the trial enrolled only those patients having a specific genotype, and certain patients who have or are willing to have a Medtronic device implanted for monitoring and recording AFB data. As a result, enrollment for GENETIC-AF was slower than expected, with our first patient enrolled in June 2014 and enrollment completed in August 2017. Because of the rigorous enrollment criteria, our clinical trial timelines were delayed from our original projections. We anticipate that any future Phase 3 clinical trial of Gencaro, including PRECISION-AF, may have similar enrollment criteria, and we cannot guarantee that we will not have similar enrollment issues in any future clinical trials.

We may also encounter difficulty enrolling a sufficient number of patients in any future clinical trial, due to circumstances which are outside our control, including as a result of the ongoing COVID-19 pandemic. See “Our business could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 global pandemic, in regions where we or third parties on which we rely have clinical trial sites or other business operations. We anticipate having clinical trial sites in countries that have been directly affected by COVID-19 and depend on third party manufacturing operations for various stages of our supply chain” for a discussion of the risks that the COVID-19 pandemic poses to, among other things, our anticipated clinical trials.

***We will rely on contract research organizations to conduct substantial portions of our clinical trials, including any future clinical trial of rNAPc2 or Gencaro, and as a result, we will be unable to directly control the timing, conduct and expense of all aspects of our clinical trials.***

We do not currently have sufficient staff with the requisite experience to conduct our clinical trials and therefore will rely on third parties to conduct certain aspects of any future clinical trials. We previously contracted with a CRO to conduct components of our GENETIC-AF clinical trial and anticipate contracting with a CRO to conduct components of any future clinical trial for Gencaro and components of the clinical study of rNAPc2 or any future clinical trials for our other product candidates. As a result, we will have less control over many details and steps of any clinical trial, the timing and completion of any clinical trial, the required reporting of adverse events and the management of data developed through any clinical trial than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties, such as CROs, may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our clinical trial. We may experience unexpected cost increases that are beyond our control. Problems with the timeliness or quality of the work of a CRO may lead us to seek to terminate the relationship and use an alternative service provider. However, making any change may be costly and may delay ongoing trials, if any, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be impossible to find a replacement organization that can conduct clinical trials in an acceptable manner and at an acceptable cost.

Even though we anticipate relying on CROs in the future, we will likely have to devote substantial resources and rely on the expertise of our employees to manage the work being done by the CROs. Due to our limited experience in managing clinical trials, we cannot guarantee our employees will do so effectively.

***We expect to depend on existing and future collaborations with third parties for the development of some of our product candidates. If those collaborations are not successful, we may not be able to complete the development of these product candidates.***

We intend to collaborate with one or more clinical trial networks in our development program for rNAPc2. As a result, we will lack direct control over certain aspects of the development program and the amount and timing of resources that these collaborators devote to the project.

We had a collaboration agreement with Medtronic that supported our GENETIC-AF clinical trial. If our arrangement with Medtronic, as amended, is continued as part of our future development of Gencaro, we will have limited control over the amount and timing of resources that they dedicate to the development of Gencaro. This is also likely to be true in any future collaboration with third parties and we may seek additional third party collaborators for the development of rNAPc2, Gencaro or any other product candidates. Our ability to benefit from these arrangements will depend on our collaborators’ abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- 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 trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result 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 elect to take over manufacturing rather than retain us as manufacturers and may encounter problems in starting up or gaining approval for their manufacturing facility and so be unable to continue development of product candidates;
- we may be required to undertake the expenditure of substantial operational, financial and management resources in connection with any collaboration;
- we may be required to issue equity securities to collaborators that would dilute our existing stockholders' percentage ownership;
- we may be required to assume substantial actual or contingent liabilities;
- collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products; and
- collaborators may experience financial difficulties.

We face a number of challenges in seeking additional collaborations. Collaborations are complex and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors, such as the design or results of our clinical trials, the potential market for our product candidates, the costs and complexities of manufacturing and delivering our product candidates to patients, the potential of competing products, the existence of uncertainty with respect to ownership or the coverage of our intellectual property, and industry and market conditions generally. If we were to determine that additional collaborations for our Gencaro development is necessary and were unable to enter into such collaborations on acceptable terms, we might elect to delay or scale back the development or commercialization of Gencaro in order to preserve our financial resources or to allow us adequate time to develop the required physical resources and systems and expertise ourselves.

Collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner, or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

***Any future clinical trial for Gencaro will require the use of a third-party diagnostic services provider to administer a genetic test needed to identify the patient receptor genotypes of clinical trial participants, and as a result, we will be unable to directly control the timing, conduct and expense of the genetic test.***

We anticipate that any future clinical trial of Gencaro, if any, will require a companion diagnostic test that identifies the patient's receptor genotype. The trial would only enroll those patients with the receptor that has the potential for enhanced efficacy, the beta-1 389 Arg receptor as detected by a beta-1 389 Arg/Arg genotype. Accordingly, we anticipate that any future clinical trial for Gencaro will require the use of a third-party diagnostic service to perform the genetic testing. There has been limited experience in our industry in prospective development of companion diagnostics required to perform the required molecular profiling. We entered into an agreement with LabCorp to provide the diagnostic services of the genetic test needed to support our GENETIC-AF clinical trial. To provide those services, LabCorp obtained from the FDA an investigational device exemption, or IDE, for the companion diagnostic test being used in our GENETIC-AF clinical trial. We would expect a similar agreement and approval would be necessary for any companion diagnostic used in any future clinical trials for Gencaro.

The FDA and similar regulatory authorities outside the United States regulate companion diagnostics. Companion diagnostics require separate or coordinated regulatory approval prior to commercialization. Changes to regulatory advice could delay our development programs or delay or prevent eventual marketing approval for our product candidates that may otherwise be approvable. In July 2011, the FDA issued draft guidance that stated that if safe and effective use of a therapeutic depends on an *in vitro* diagnostic, the FDA generally will not approve the therapeutic unless the FDA approves or clears this "*in vitro* companion diagnostic device" at the same time that the FDA approves the therapeutic. The approval or clearance of the companion diagnostic would occur through the FDA's Center for Devices and Radiological Health. In 2014, the FDA issued guidance on in vitro companion diagnostic devices. The guidance allows for flexibility by the FDA in the case of therapeutic products to treat serious conditions for which no alternative treatment exists and the benefits of using the companion diagnostic outweigh the risk, but it is unclear how this discretion may be applied by the agency with respect to the companion diagnostic test related to any Gencaro clinical trials. The FDA's evolving position on the topic of companion diagnostics could affect our clinical development programs that utilize companion diagnostics. In particular, the FDA may limit our ability to use retrospective data, otherwise disagree with our approaches to trial design, biomarker qualification, clinical and analytical validity, and clinical utility, or make us repeat aspects of a trial or initiate new trials.

Given our limited experience in developing diagnostics, we expect to rely primarily on third parties for the design and manufacture of the companion diagnostics for our product candidates. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our product candidates that require such diagnostics, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not receive marketing approval and we may not realize the full commercial potential of any products that receive marketing approval. As a result, our business could be materially harmed.

***We will need to establish a collaborative arrangement with a third-party diagnostics services provider to obtain marketing clearance or approval of the companion genetic test for Gencaro. There is no guarantee that the FDA will grant timely clearance or approval of the genetic test, if at all, and failure to obtain such timely clearance or approval would adversely affect our ability to market Gencaro.***

The drug label we intend to seek for Gencaro would identify the patient receptor genotype for which the drug is approved. Accordingly, we believe developing a genetic test that is simple to administer and widely available will be critical to the successful commercialization of Gencaro. The genetic test will be subject to regulation by the FDA and by comparable agencies in various foreign countries. The process of complying with the requirements of the FDA and comparable agencies is costly, time consuming and burdensome.

Despite the time and expense expended, regulatory clearance or approval is never guaranteed. If regulatory clearance or approval is delayed, or if one or more third-party diagnostic services providers are unable to obtain FDA approval of the genetic test at all or in parallel with the approval of Gencaro, or are unable to commercialize the test successfully and in a manner that effectively supports the commercial efforts for Gencaro, or if the information concerning the differential response to Gencaro resulting from certain genetic variation is not included in the approval label for Gencaro, the commercial launch of Gencaro may be significantly and adversely affected.

***Regulatory approval is required for the genetic test to be used in our Gencaro clinical trials and to support the commercialization of the test, if approved. Delays or failures in obtaining such regulatory approval, including any required validation analyses may prevent a third-party diagnostics provider from commercializing such genetic test and will adversely affect our business, operating results and prospects.***

Before a genetic test can be used commercially, including in conjunction with Gencaro, if it is approved for marketing, the third-party diagnostics provider must obtain FDA Premarket Approval, or PMA, for such test. The FDA may require additional validation of the genetic test we used in GENETIC-AF prior to any approval of Gencaro or the genetic test or prior to the use of such test in any future clinical trials for Gencaro. We anticipate the genetic test will be required as a condition to prescribing Gencaro. There is no guarantee the FDA will approve the anticipated PMA submission for the genetic test. Even if the genetic test is eventually approved, performing additional validation work necessary to support the PMA, if required, for current or future genetic test products, including one associated with Gencaro, would require additional time and expense and the outcome would be uncertain. Moreover, such delays or increased costs or failures could adversely affect our business, operating results and prospects for commercializing the genetic test.

***If a third-party diagnostics provider responsible for the genetic test associated with Gencarp or certain of its third-party suppliers fails to comply with ongoing FDA or other foreign regulatory authority requirements, or if there are unanticipated problems with the genetic test, these products could be subject to restrictions or withdrawal from use in a trial or from the market.***

Any diagnostic for which a third-party diagnostics provider obtains clearance or approval, and the manufacturing processes, reporting requirements, post-approval clinical data and promotional activities for such product, will be subject to continued regulatory review, oversight and periodic inspections by the FDA and other domestic and foreign regulatory bodies. With respect to the genetic test, to the extent applicable, any third-party diagnostics provider and certain of its suppliers will be required to comply with the FDA's Quality System Regulation, or QSR, and International Standards Organization, or ISO, requirements which cover the methods and documentation of the design, testing, production, control, quality assurance, labeling, packaging, storage and shipping of any product for which clearance or approval is obtained. Regulatory bodies, such as the FDA, enforce the QSR and other regulations through periodic inspections. The failure by a third-party diagnostics provider, or certain of its third-party manufacturers or suppliers, as the case may be, to comply with applicable statutes and regulations administered by the FDA and other regulatory bodies, or the failure to timely and adequately respond to any adverse inspectional observations or product safety issues, could result in, among other things, enforcement actions. If any of these actions were to occur, it could harm our reputation and cause product sales and profitability of Gencaro, if approved, to suffer and may prevent us from generating revenue or utilizing the genetic test further in any clinical trial. Even if regulatory clearance or approval is granted, such clearance or approval may be subject to limitations on the intended uses for which the product may be marketed and reduce our potential to successfully commercialize the product and generate revenue from the product.

***Future sales of Gencaro may suffer if its marketplace acceptance is negatively affected by the genetic test.***

The genetic test is an important component of the commercial strategy for Gencaro in addition to being required for our clinical trials. We believe that the genetic test helps predict patient response to Gencaro, and that this aspect of the drug is important to its ability to compete effectively with current therapies. The genetic test adds an additional step in the prescribing process, an additional cost for the patient and payors, the risk that the test results may not be rapidly available and the possibility that it may not be available at all to hospitals and medical centers. Although we anticipate that Gencaro, if approved in a timely manner, would be the first genetically-targeted cardiovascular drug, Gencaro will be one of a number of successful drugs in the beta-blocker class currently on the market. Prescribers may be more familiar with these other beta-blockers, and may be resistant to prescribing Gencaro as an AF therapy in patients with HF. For instance, the top-line results of our Phase 2B GENETIC-AF clinical trial indicated that Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate (TOPROL-XL). If our future clinical trials in Gencaro do not show that Gencaro has a clear therapeutic benefit as compared to other drugs in the beta-blocker class currently on the market, then prescribers may be unlikely to prescribe Gencaro to patients, even if approved. Any one of these factors could affect prescriber behavior, which in turn may substantially impede market acceptance of the genetic test, which could cause significant harm to Gencaro's ability to compete, and in turn harm our business.

***Unless we are able to generate sufficient product revenue, we will continue to incur losses from operations and will not achieve or maintain profitability. We are years away from commercializing a product and generating product revenue.***

Our historical losses have had and will continue to have an adverse effect on our stockholders' equity and working capital, among other things. We are years away from commercializing a product and generating any product revenue. As a result, we expect to continue to incur significant operating losses for the foreseeable future. Even if we ultimately receive regulatory approval for rNAPc2, Gencaro or our other product candidates, sales of such products may not generate sufficient revenue for it to achieve or maintain profitability. Because of the numerous risks and uncertainties associated with developing therapeutic drugs, we may experience larger than expected future losses and may never reach profitability.

***Our product candidates are subject to extensive regulation, which can be costly and time-consuming, and unsuccessful or delayed regulatory approvals could increase our future development costs or impair our future revenue.***

The preclinical and clinical development, testing, manufacture, safety, efficacy, labeling, storage, recordkeeping, and subsequent advertising, promotion, sale, marketing, and distribution, if approved, of our product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and elsewhere. These regulations also vary in important, meaningful ways from country to country. We are not permitted to market a potential drug in the United States until we receive approval of an NDA from the FDA for such drug. We have not received an NDA approval from the FDA for rNAPc2, Gencaro or any of our other product candidates. There can be no guarantees with respect to our product candidates that clinical studies will adequately support an NDA, that the products will receive necessary regulatory approvals, or that they will prove to be commercially successful.

To receive regulatory approval for the commercial sale of any product candidates, we must demonstrate safety and efficacy in humans to the satisfaction of regulatory authorities through preclinical studies and adequate and well-controlled clinical trials of the product candidates. This process is expensive and can take many years, and failure can occur at any stage of the testing. Our failure to adequately demonstrate the safety and efficacy of our product candidates will prevent regulatory approval and commercialization of such products.

In 2008, we submitted and the FDA accepted our NDA filing for Gencaro for the treatment of chronic HF. In 2009, the FDA issued a Complete Response Letter, or CRL, in which the FDA stated that it could not approve the Gencaro NDA in its current form and specified actions required for approval of the NDA, including conducting an additional Phase 3 clinical trial of Gencaro in patients with HF. We completed a Phase 2B clinical study of Gencaro in HF patients to assess its efficacy in reducing or preventing AF. We enrolled 267 HF patients with AF in the Phase 2B clinical trial. We reported top-line Phase 2B data in February 2018. In the third quarter of 2018, we submitted a SPA to the FDA for a Phase 3 clinical trial. In 2019, the FDA approved our SPA request for a Phase 3 clinical trial of Gencaro. Even though the FDA approved our SPA, this product candidate will require years of additional clinical development. Even if we conduct additional studies in accordance with our SPA agreement or further FDA guidance and submit or file a new or amended NDA, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

In the event that we or our collaborators conduct preclinical studies that do not comply with Good Laboratory Practices, or GLP, or incorrectly design or carry out human clinical trials in accordance with Good Clinical Practices, or GCP, or those clinical trials fail to demonstrate clinical significance, it is unlikely that we will be able to obtain FDA approval for product development candidates. Our inability to successfully initiate and effectively complete clinical trials for any product candidate on schedule, or at all, will severely harm our business. Significant delays in clinical development could materially increase product development costs or allow our competitors to bring products to market before we do, impairing our ability to effectively commercialize any future product candidate. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including:

- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidates for use in trials;
- failure of clinical materials to meet pre-established specifications at product release or during ongoing stability studies;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board to conduct a clinical trial at a prospective study site;
- delays in recruiting patients to participate in a clinical trial, which may be due to the size of the patient population, eligibility criteria, protocol design, perceived risks and benefits of the drug, availability of other approved and standard of care therapies or, availability of clinical trial sites;
- other clinical trials seeking to enroll subjects with similar profile;
- failure of our clinical trials and clinical investigators to be in compliance with GCP;
- unforeseen safety issues, including negative results from ongoing preclinical studies;
- inability to monitor patients adequately during or after treatment;
- difficulty recruiting and monitoring multiple study sites;
- failure of our third-party contract research organizations, clinical site organizations and other clinical trial managers, to satisfy their contractual duties, comply with regulations or meet expected deadlines; and

- an insufficient number of patients who have, or are willing to have, a Medtronic device implanted for monitoring and recording AF burden data.

In addition, any approvals we may obtain may not cover all of the clinical indications for which we seek approval or permit us to make claims of superiority over currently marketed competitive products. Also, an approval might contain significant limitations in the form of narrow indications, warnings, precautions or contraindications with respect to conditions of use. If the FDA determines that a risk evaluation and mitigation strategy, or REMS, is necessary to ensure that the benefits of the drug outweigh the risks, we may be required to include as part of the NDA a proposed REMS that may include a package insert directed to patients, a plan for communication with healthcare providers, restrictions on a drug's distribution, or a Medication Guide, to provide better information to consumers about the drug's risks and benefits. Finally, an approval could be conditioned on our commitment to conduct further clinical trials, which we may not have the resources to conduct or which may negatively impact our financial situation.

The manufacture and analytical testing of rNAPc2 and Gencaro is performed by third party suppliers, who must also meet cGMP requirements and pass a pre-approval inspection of their facilities before we can obtain marketing approval.

All of our product candidates are prone to the risks of failure inherent in drug development. The results from preclinical animal testing and early human clinical trials may not be predictive of results obtained in later human clinical trials. Further, although a new product may show promising results in preclinical or early human clinical trials, it may subsequently prove unfeasible or impossible to generate sufficient safety and efficacy data to obtain necessary regulatory approvals. The data obtained from preclinical and clinical studies are susceptible to varying interpretations that may delay, limit or prevent regulatory approval, and the FDA and other regulatory authorities in the United States and elsewhere exercise substantial discretion in the drug approval process. The numbers, size and design of preclinical studies and clinical trials that will be required for FDA or other regulatory approval will vary depending on the product candidate, the disease or condition for which the product candidate is intended to be used and the regulations and guidance documents applicable to any particular product candidate. The FDA or other regulators can delay, limit or deny approval of any product candidate for many reasons, including, but not limited to:

- side effects;
- safety and efficacy;
- defects in the design of clinical trials;
- the fact that the FDA or other regulatory officials may not approve our or our third party manufacturer's processes or facilities; or
- the fact that new regulations may be enacted by the FDA or other regulators may change their approval policies or adopt new regulations requiring new or different evidence of safety and efficacy for the intended use of a product candidate.

In light of widely publicized events concerning the safety of certain drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of certain drug products, revisions to certain drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and approval. Data from clinical trials may receive greater scrutiny with respect to safety and the product's risk/benefit profile, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense, and a delay or failure in obtaining approval or approval for a more limited indication than originally sought. Aside from issues concerning the quality and sufficiency of submitted preclinical and clinical data, the FDA may be constrained by limited resources from reviewing and determining the approvability of the Gencaro NDA in a timely manner.

In pursuing clinical development of Gencaro for an AF indication, we will be required to amend the Gencaro HF NDA or prepare a new NDA. The FDA could approve Gencaro, but without including some or all of the prescribing information that we have requested. For instance, the FDA could approve Gencaro for AF in a more limited patient population or include additional warnings in the drug's label. This, in turn, could substantially and detrimentally impact our ability to successfully commercialize Gencaro and effectively protect our intellectual property rights in Gencaro.

***If our product candidates receive regulatory approval, we would be subject to ongoing regulatory obligations and restrictions, which may result in significant expenses and limit our ability to develop and commercialize other potential products.***

If a product candidate of ours is approved by the FDA or by another regulatory authority, we would be held to extensive regulatory requirements over product manufacturing, testing, distribution, labeling, packaging, adverse event reporting and other reporting to regulatory authorities, storage, advertising, marketing, promotion, distribution, and record keeping. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the product candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Previously unknown problems with the product candidate, including adverse events of unanticipated severity or frequency, may result in additional regulatory controls or restrictions on the marketing or use of the product or the need for post marketing studies, and could include suspension or withdrawal of the products from the market.

Furthermore, our third-party manufacturers and the manufacturing facilities that they use to make our product candidates are regulated by the FDA. Quality control and manufacturing procedures must continue to conform to cGMP after approval. Drug manufacturers and their subcontractors are required to register their facilities and products manufactured annually with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA, state and/or other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product, or on the manufacturing or laboratory facility, including a withdrawal of the drug from the market or suspension of manufacturing. Any changes to an approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our third-party manufacturers will also be subject to ongoing FDA requirements for submission of safety and other post-market information.

The marketing and advertising of our drug products by our collaborators or us will be regulated by the FDA, certain state agencies or foreign regulatory authorities. Violations of these laws and regulations, including promotion of our products for unapproved uses or failing to disclose risk information, are punishable by criminal and civil sanctions and may result in the issuance of enforcement letters or other enforcement action by the FDA, U.S. Department of Justice, state agencies, or foreign regulatory authorities that could jeopardize our ability to market the product.

In addition to the FDA, state or foreign regulations, the marketing of our drug products by us or our collaborators will be regulated by federal, state or foreign laws pertaining to health care “fraud and abuse,” such as the federal anti-kickback law prohibiting bribes, kickbacks or other remuneration for the order or recommendation of items or services reimbursed by federal health care programs. Many states have similar laws applicable to items or services reimbursed by commercial insurers. Violations of these laws are punishable by criminal and civil sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state health care programs, including the Medicare, Medicaid and Veterans Affairs healthcare programs. Because of the far-reaching nature of these laws, we may be required to discontinue one or more of our practices to be in compliance with these laws. Healthcare fraud and abuse regulations are complex, and even minor irregularities can potentially give rise to claims that a statute or prohibition has been violated. Any violations of these laws, or any action against us for violations of these laws, even if we successfully defend against it, could have a material adverse effect on our business, financial condition and results of operations.

We could also become subject to false claims litigation under federal statutes, which can lead to civil money penalties, restitution, criminal fines and imprisonment, and exclusion from participation in Medicare, Medicaid and other federal and state health care programs. These false claims statutes include the False Claims Act, which allows any person to bring a suit on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, under federal programs or contracts claims or other violations of the statute and to share in any amounts paid by the entity to the government in fines or settlement. These suits against pharmaceutical companies have increased significantly in volume and breadth in recent years. Some of these suits have been brought on the basis of certain sales practices promoting drug products for unapproved uses. This new growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay fines or restitution, or be excluded from the Medicare, Medicaid, Veterans Affairs and other federal and state healthcare programs as a result of an investigation arising out of such action. We may become subject to such litigation and, if we are not successful in defending against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations. We could also become subject to false claims litigation and consumer protection claims under state statutes, which also could lead to civil monetary penalties, restitution, criminal fines and imprisonment, and exclusion from participation in state health care programs. Of note, over the past few years there has been an increased focus on the sales and marketing practices of the pharmaceutical industry at both the federal and state level. Additionally, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements may be enacted or additional regulations may be adopted that could prevent or delay regulatory approval of our product candidates or limit our ability to commercialize our products. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere.

If we, our collaborators or our third-party manufacturers fail to comply with applicable continuing regulatory requirements, our business could be seriously harmed because a regulatory agency may:

- issue untitled or warning letters;
- suspend or withdraw our regulatory approval for approved products;
- seize or detain products or recommend a product recall of a drug or medical device, or issue a mandatory recall of a medical device;
- refuse to approve pending applications or supplements to approved applications filed by us;
- suspend our ongoing clinical trials;
- restrict our operations, including costly new manufacturing requirements, or restrict the sale, marketing and/or distribution of our products;
- seek an injunction;
- pursue criminal prosecutions;
- close the facilities of our contract manufacturers; or
- impose civil or criminal penalties.

***Reliance on third parties to commercialize rNAPc2, Gencaro or our other product candidates could negatively impact our business. If we are required to establish a direct sales force in the United States and are unable to do so, our business may be harmed.***

Commercialization of rNAPc2, Gencaro or any other product candidate, if approved, particularly the establishment of a sales organization, will require substantial additional capital resources. We currently intend to pursue a strategic partnership alternative for the commercialization of rNAPc2 or Gencaro, if it is approved, and we have suspended our efforts to build internal sales, marketing and distribution capabilities. If we elect to rely on third parties to sell rNAPc2, Gencaro and any other products, then we may receive less revenue than if we sold such products directly. In addition, we may have little or no control over the sales efforts of those third parties. If we are unable to complete a strategic transaction, we would be unable to commercialize rNAPc2, Gencaro or any other product candidate without substantial additional capital. Even if such capital were secured, we would be required to build internal sales, marketing and distribution capabilities to market rNAPc2 or Gencaro in the United States. None of our current employees have experience in establishing and managing a sales force.

In the event we are unable to sell rNAPc2, Gencaro and other selected product candidates, either directly or through third parties via a strategic transaction, the commercialization of rNAPc2 or Gencaro, if approved, may be delayed indefinitely.

***We are dependent on our key personnel.***

The success of our business is highly dependent on the principal members of our board of directors and executive management, including our President and Chief Executive Officer, Michael R. Bristow. The loss of the services of any such individual might seriously harm our product development, partnering and financing efforts. Recruiting and training personnel with the requisite skills is challenging and we compete for talent with companies that are larger and have more financial resources.

***We have no manufacturing capacity which puts us at risk of lengthy and costly delays of bringing our products to market.***

We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates, including their drug substance or active pharmaceutical ingredients, or API. We have no experience in drug formulation or manufacturing, and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We do not intend to develop facilities for the manufacture of product candidates for clinical trials or commercial purposes in the foreseeable future. We have contracted with several third-party manufacturing organizations for production and analytical testing of our product candidates. These contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our products. In addition, these manufacturers may have staffing difficulties, may experience delays due to key material or component availability, may not be able to manufacture our products on a timely basis or may become financially distressed. In the event of errors in forecasting production quantities required to meet demand, natural disaster, equipment malfunctions or failures, technology malfunctions, strikes, lock-outs or work stoppages, regional power outages, product tampering, war or terrorist activities, actions of regulatory authorities, business failure, strike or other difficulty, we may be unable to find an alternative third-party manufacturer in a timely manner and the production of our product candidates would be interrupted, resulting in delays and additional costs, which could impact our ability to commercialize and sell our product candidates. We or our contract manufacturers may also fail to achieve and maintain required manufacturing standards, which could result in patient injury or death, product recalls or withdrawals, an order by governmental authorities to halt production, delays or failures in product testing or delivery, stability testing failures, cost overruns or other problems that could seriously hurt our business. Contract manufacturers also often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. In addition, our contract manufacturers are subject to ongoing inspections and regulation by the FDA, the U.S. Drug Enforcement Agency and corresponding foreign and state agencies and they may fail to meet these agencies' acceptable standards of compliance. If our contract manufacturers fail to comply with applicable governmental regulations, such as quality control, quality assurance and the maintenance of records and documentation, we may not be able to continue production of the API or finished product. If the safety of any API or product supplied is compromised due to failure to adhere to applicable laws or for other reasons, this may jeopardize our regulatory approval for rNAPc2, Gencaro and other product candidates, and we may be held liable for any injuries sustained as a result. Upon the occurrence of one of the aforementioned events, the ability to switch manufacturers may be difficult for a number of reasons, including:

- the number of potential manufacturers is limited and we may not be able to negotiate agreements with alternative manufacturers on commercially reasonable terms, if at all;
- long lead times are often needed to manufacture drugs;
- the manufacturing process is complex and may require a significant learning curve; and
- the FDA must approve any replacement prior to manufacturing, which requires new testing and compliance inspections.

***Transitioning from a clinical development stage company will require successful completion of a number of steps, many of which are outside of our control and, consequently, we can provide no assurance of our successful and timely transition from a clinical development stage company.***

We are a clinical development stage biopharmaceutical company with a limited operating history. To date we have not generated any product revenue and have historically funded our operations through investment capital. Our future growth depends on our ability to emerge from the clinical development stage and successfully commercialize or provide for the commercialization of rNAPc2, Gencaro and our other product candidates which in turn, will depend, among other things, on our ability to:

- conduct additional clinical trials and develop and obtain regulatory approval for rNAPc2, Gencaro or other product candidates;
- successfully partner a companion genetic test with the commercial launch of rNAPc2 or Gencaro;
- enter into a strategic transaction enabling the continued development and commercialization of rNAPc2 or Gencaro, or alternatively, raise significant additional capital to enable these activities;
- pursue additional indications for rNAPc2 or Gencaro and develop other product candidates, including other cardiovascular therapies; and
- obtain commercial quantities of rNAPc2, Gencaro or other product candidates at acceptable cost levels.

Any one of these factors or other factors discussed in this report could affect our ability to successfully commercialize Gencaro and other product candidates, which could impact our ability to earn sufficient revenues to transition from a clinical development stage company and continue our business.

***If approved by the FDA, rNAPc2 or Gencaro will be entering a competitive marketplace and may not succeed.***

We do not yet know what the commercial opportunity will be, if any, for rNAPc2 if it is approved for treating COVID-19 disease. We do not know how and to whom rNAPc2 would be marketed and what the commercial arrangements would be for its sales and reimbursement. While we anticipate that rNAPc2, if approved, could potentially be used in combination with antiviral drugs and other therapies, there are other vaccines and therapies under development.

Gencaro is a new type of beta-blocker and vasodilator being developed for AF. While we anticipate that this drug, if approved, would be the first genetically-targeted cardiovascular drug, and potentially the only beta-blocker approved for AF, Gencaro will be one of a number of accepted treatments for AF. In addition, our proposed prescribing information for Gencaro is expected to include a requirement for genetic testing of the patient to ascertain if they have the genotype that we believe responds best to Gencaro. This additional step will add incremental cost and procedures to prescribing Gencaro, which could make it more difficult to compete against existing therapies.

Our commercial opportunity may be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than Gencaro. If products with any of these properties are developed, or any of the existing products are better marketed, then prescriptions of Gencaro by physicians and patient use of Gencaro could be significantly reduced or rendered obsolete and noncompetitive. Further, public announcements regarding the development of any such competing drugs could adversely affect the market price of our common stock and the value of our assets.

***Future sales of our products may suffer if they are not accepted in the marketplace by physicians, patients and the medical community.***

rNAPc2, Gencaro or our other product candidates may not gain market acceptance among physicians, patients and the medical community. The degree of market acceptance of rNAPc2, Gencaro or our other product candidates will depend on a number of factors, such as its effectiveness and tolerability, as compared with competitive drugs. For instance, if rNAPc2 is approved, by that time there may be superior alternatives in terms of vaccines and/or therapeutics that may significantly impact the relative medical benefits offered by rNAPc2. If our future clinical trials for rNAPc2 do not show that rNAPc2 has a clear therapeutic benefit as compared to other therapies or vaccines that are approved in the interim, then there may be a limited or no commercial market for rNAPc2. Also, prevalence and severity of side-effects could negatively affect market acceptance of rNAPc2. Failure to achieve market acceptance of rNAPc2 or Gencaro would significantly harm our business.

If we are unable to obtain acceptable prices or adequate reimbursement from third-party payors for rNAPc2, Gencaro, or any other product candidates that we may seek to commercialize, then our revenues and prospects for profitability will suffer.

Our or any strategic partner’s ability to commercialize rNAPc2, Gencaro, or any other product candidates that we may seek to commercialize, is highly dependent on the extent to which coverage and reimbursement for these product candidates will be available from:

- governmental payors, such as Medicare and Medicaid;
- private health insurers, including managed-care organizations; and
- other third-party payors.

Many patients will not be capable of paying for our potential products themselves and will rely on third-party payors to pay for their medical needs. A primary current trend in the U.S. health care industry is toward cost containment. Large private payors, managed-care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products.

Cost-control initiatives could decrease the price we might establish for products, which could result in product revenues lower than anticipated. If the prices for our product candidates decrease, or if governmental and other third-party payors do not provide adequate coverage and reimbursement levels, then our revenue and prospects for profitability will suffer.

***Health care reform measures could materially and adversely affect our business.***

The business and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third-party payors to contain or reduce the costs of health care. The U.S. Congress has enacted legislation to reform the health care system. While we anticipate that this legislation may, over time, increase the number of patients who have insurance coverage for pharmaceutical products, it also imposes cost containment measures that may adversely affect the amount of reimbursement for pharmaceutical products. These measures include increasing the minimum rebates for products covered by Medicaid programs and extending such rebates to drugs dispensed to Medicaid beneficiaries enrolled in Medicaid managed care organizations as well as expansion of the 340(B) Public Health Services drug discount program. In addition, such legislation contains a number of provisions designed to generate the revenues necessary to fund the coverage expansion, including new fees or taxes on certain health-related industries, including medical device manufacturers. Each medical device manufacturer has to pay an excise tax (or sales tax) in an amount equal to 2.3% of the price for which such manufacturer sells its medical devices. Such excise taxes may impact any potential sales of the genetic test if it is approved for marketing. On January 22, 2018, legislation was enacted suspending the medical device tax in 2018 and 2019. In December 2019, a permanent repeal of the medical device tax was enacted. The Gencaro Test is likely to be subject to this tax if this tax is reinstated in the future. In foreign jurisdictions there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the health care system. For example, in some countries other than the United States, pricing of prescription drugs is subject to government control and we expect to see continued efforts to reduce healthcare costs in international markets.

Some states are also considering legislation that would control the prices of drugs, and state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Managed care organizations continue to seek price discounts and, in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for drugs. It is likely that federal and state legislatures and health agencies will continue to focus on additional health care reform in the future although we are unable to predict what additional legislation or regulation, if any, relating to the health care industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation or regulation would have on our business. We or any strategic partner’s ability to commercialize rNAPc2, Gencaro, or any other product candidates that we may seek to commercialize, is highly dependent on the extent to which coverage and reimbursement for these product candidates will be available from government payors, such as Medicare and Medicaid, private health insurers, including managed care organizations, and other third-party payors, and any change in reimbursement levels could materially and adversely affect our business. Further, the pendency or approval of future proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to obtain strategic partnerships or licenses.

***Our competitors may be better positioned in the marketplace and thereby may be more successful than us at developing, manufacturing and marketing approved products.***

Many of our competitors currently have significantly greater financial resources and expertise in conducting clinical trials, obtaining regulatory approvals, managing manufacturing and marketing approved products than us. Other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. In addition, these third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring therapies and therapy licenses complementary to our programs or advantageous to our business. We expect that our ability to compete effectively will depend upon our ability to:

- successfully and rapidly complete clinical trials for any product candidates and obtain all requisite regulatory approvals in a cost-effective manner;
- build an adequate sales and marketing infrastructure, raise additional funding, or enter into strategic transactions enabling the commercialization of our products;
- develop competitive formulations of our product candidates;
- attract and retain key personnel; and
- identify and obtain other product candidates on commercially reasonable terms.

***If we fail to identify and license or acquire other products or product candidates, then we may be unable to expand our business, and the acquisition or licensing of other products or product candidates may put a strain on our operations and will likely require us to seek additional financing.***

One of our strategies is to license or acquire clinical-stage products or product candidates and further develop them for commercialization. The market for licensing and acquiring products and product candidates is intensely competitive and many of our competitors may have greater resources than we do. If we undertake any additional acquisitions, whether of product candidates or other biopharmaceutical companies, the process of integrating an acquired product candidate or complementary company into our business may put a strain on our operations, divert personnel, financial resources and management's attention. In 2020, our research and development activities were dedicated to initiating the clinical trial of rNAPc2. If we are not able to substantially expand our research and development efforts, or identify, or license or acquire other products or product candidates or complete future acquisitions, then we will likely be unable expand our pipeline of product candidates. In addition, any future acquisition would give rise to additional operating costs and will likely require us to seek additional financing. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results.

***We would be subject to applicable regulatory approval requirements of the foreign countries in which we market our products, which are costly and may prevent or delay us from marketing our products in those countries.***

In addition to regulatory requirements in the United States, we would be subject to the regulatory approval requirements in each foreign country where we market our products. In addition, we might be required to identify one or more collaborators in these foreign countries to develop, seek approval for and manufacture our products and any companion genetic test for Gencaro. If we decide to pursue regulatory approvals and commercialization of our product candidates internationally, we may not be able to obtain the required foreign regulatory approvals on a timely basis, if at all, and any failure to do so may cause us to incur additional costs or prevent us from marketing our products in foreign countries, which may have a material adverse effect on our business, financial condition and results of operations.

***If our internal control over financial reporting is not considered effective, our business and stock price could be adversely affected.***

Section 404 of the Sarbanes-Oxley Act of 2002 requires us to evaluate the effectiveness of our internal control over financial reporting as of the end of each fiscal year, and to include a management report assessing the effectiveness of our internal control over financial reporting in our annual report on Form 10-K for that fiscal year. Our management, including our principal executive officer and principal financial officer, does not expect that our internal control over financial reporting will prevent all error and all fraud. We continue to operate with a small staff for financial reporting. Though the process and design of our internal controls over financial reporting have not been altered, the small number of staff involved in financial reporting may limit our ability to properly segregate internal control procedures which could result in deficiencies or material weaknesses in our internal controls in the future. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud involving a company have been, or will be, detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and we cannot assure you that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become ineffective because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected. We cannot assure you that we or our independent registered public accounting firm will not identify a material weakness in our internal control over financial reporting in the future. A material weakness in our internal control over financial reporting would require management to consider our internal control over financial reporting as ineffective. If our internal control over financial reporting is not considered effective, we may experience a loss of public confidence, which could have an adverse effect on our business and on the market price of our common stock.

***Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.***

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of our domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, significantly revised the Internal Revenue Code of 1986, as amended, or the Code. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Cuts and Jobs Act may affect us, and certain aspects of the Tax Cuts and Jobs Act could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Cuts and Jobs Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

***Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.***

As of December 31, 2020, we had net operating loss, or NOL, carryforwards of approximately $179.5 million, and approximately $1.9 million of research and development credits that may be used to offset future taxable income. Our net operating loss carryforwards generated prior to 2018 will expire beginning in 2025 if not utilized. Under the Tax Cuts and Jobs Act, U.S. federal NOLs incurred in tax years ending after December 31, 2017, may be carried forward indefinitely, but the deductibility of federal NOLs generated in tax years beginning after December 31, 2017, may be limited. In general, under Section 382 of the Code, a corporation that undergoes an “ownership change” (as defined under Section 382 of the Code and applicable Treasury Regulations) is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. We have not determined whether we have experienced an ownership change in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes. For these reasons, we may not be able to utilize a material portion of the NOLs reflected on our balance sheet, even if we attain profitability, which could potentially result in increased future tax liability to us and could adversely affect our operating results and financial condition.

***Security breaches, cyber-attacks, or other disruptions or incidents could expose us to liability and affect our business and reputation.***

We are increasingly dependent on our information technology systems and infrastructure for our business. We, our collaborators and our service providers collect, store, and transmit sensitive information including intellectual property, proprietary business information, clinical trial data and personal information in connection with our business operations. The secure maintenance of this information is critical to our operations and business strategy. Some of this information could be an attractive target of criminal attack by third parties with a wide range of motives and expertise, including organized criminal groups, “hacktivists,” patient groups, disgruntled current or former employees, nation-state and nation-state supported actors, and others. Cyber-attacks are of ever-increasing levels of sophistication, and despite our security measures, our information technology and infrastructure may be vulnerable to such attacks or may be breached, including due to employee error or malfeasance.

We have implemented information security measures to protect our systems, proprietary information and sensitive data against the risk of inappropriate and unauthorized external use and disclosure and other types of compromise. However, despite these measures, and due to the ever changing information cyber-threat landscape, we cannot guarantee that these measures will be adequate to detect, prevent or mitigate security breaches and other incidents and we may be subject to data breaches through cyber-attacks, malicious code (such as viruses and worms), phishing attacks, social engineering schemes, and insider theft or misuse. Any such breach could compromise our networks and the information stored there could be accessed, modified, destroyed, publicly disclosed, lost or stolen. If our systems become compromised, we may not promptly discover the intrusion.

Any security breach of other incident, whether real or perceived, could cause us to suffer reputational damage. Such incidents could result in costs to respond to, investigate and remedy such incidents, notification obligations to affected individuals, government agencies, credit reporting agencies and other third parties, legal claims or proceedings, and liability under our contracts with other parties and federal and state laws that protect the privacy and security of personal information. Any one of these events could cause our business to be materially harmed and our results of operations would be adversely impacted.

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

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended, or HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

In addition, the California Consumer Privacy Act, or the CCPA, became effective on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although there are limited exemptions for clinical trial data and the CCPA's implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, the CCPA may increase our compliance costs and potential liability. Many similar privacy laws have been proposed at the federal level and in other states.

Foreign data protection laws, including, without limitation, the European Union Directive 95/46/EC, or the Directive, and the European Union's General Data Protection Regulation, or the GDPR, that became effective in May 2018, and member state data protection legislation, may also apply to health-related and other personal information obtained outside of the United States. These laws impose strict obligations on the ability to process health-related and other personal information of data subjects in the European Union and the United Kingdom, including in relation to use, collection, analysis, and transfer (including cross-border transfer) of such personal information. These laws include several requirements relating to the consent of the individuals to whom the personal data relates, limitations on data processing, establishing a legal basis for processing, notification of data processing obligations or security incidents to appropriate data protection authorities or data subjects, the security and confidentiality of the personal data and various rights that data subjects may exercise.

The Directive and the GDPR prohibit, without an appropriate legal basis, the transfer of personal data to countries outside of the European Economic Area, or EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the United States, uncertainty about compliance with European Union data protection laws remains. For example, ongoing legal challenges in Europe to the mechanisms allowing companies to transfer personal data from the EEA to the United States could result in further limitations on the ability to transfer personal data across borders, particularly if governments are unable or unwilling to reach new or maintain existing agreements that support cross-border data transfers, such as the European Union-U.S. and Swiss-U.S. Privacy Shield framework. Additionally, other countries have passed or are considering passing laws requiring local data residency.

Under the GDPR, regulators may impose substantial fines and penalties for non-compliance. Companies that violate the GDPR can face fines of up to the greater of 20 million Euros or 4% of their worldwide annual turnover (revenue). The GDPR increases our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR and other EU and international data protection rules.

Compliance with U.S. and foreign privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. Failure to comply with U.S. and foreign data protection laws and regulations could result in government investigations and enforcement actions (which could include civil or criminal penalties), fines, private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

**Risks Related to Intellectual Property and Other Legal Matters**

***If product liability lawsuits are successfully brought against us, then we will incur substantial liabilities and may be required to limit commercialization of rNAPc2, Gencaro or other product candidates.***

We face product liability exposure related to the testing of our product candidates in human clinical trials, and may face exposure to claims by an even greater number of persons once we begin marketing and distributing our products commercially. If we cannot successfully defend against product liability claims, then we will incur substantial liabilities.

Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our products and product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- substantial monetary awards to patients and others;
- loss of revenues; and
- the inability to commercialize our products and product candidates.

We have obtained limited product liability insurance coverage. Such coverage, however, may not be adequate or may not continue to be available to us in sufficient amounts or at an acceptable cost, or at all. We may not be able to obtain commercially reasonable product liability insurance for any product candidate.

***Defending against claims relating to improper handling, storage or disposal of hazardous chemicals, radioactive or biological materials could be time consuming and expensive.***

Our research and development of product candidates may involve the controlled use of hazardous materials, including chemicals, radioactive and biological materials. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from the materials. Various laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued or be required to pay fines for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

***The loss of any rights to market key products would significantly impair our operating results.***

Our patent portfolios relating to Gencaro, including a patent that issued in 2021, are either owned by us or are subject to licenses that impose no royalty obligations or milestone payments relating to the further development, approval and commercialization of Gencaro.

Termination of our license agreements could result in the loss of our further rights to develop and commercialize Gencaro for any indication. The termination of any such license, or of any other agreement which enables us to market a key product or product candidate, could significantly and adversely affect our business.

Certain intellectual property licensed by us is the subject of additional licensing arrangements to which the party that has licensed rights to us is subject. If such parties were to breach the terms of such licenses or such licenses were otherwise to terminate, our and our partners' rights to use such technology and develop and commercialize their products such as the genetic test may terminate and our business would be materially harmed.

***Third parties may own or control patents or patent applications that we may be required to license to commercialize our product candidates or that could result in litigation that would be costly and time consuming.***

Our or any strategic partner's ability to commercialize rNAPc2, Gencaro and other product candidates depends upon our ability to develop, manufacture, market and sell these drugs without infringing the proprietary rights of third parties. A number of pharmaceutical and biotechnology companies, universities and research institutions have or may be granted patents that cover technologies similar to the technologies owned by or licensed to us. We may choose to seek, or be required to seek, licenses under third party patents, which would likely require the payment of license fees or royalties or both. We may also be unaware of existing patents that may be infringed by rNAPc2 or Gencaro, the genetic testing we intend to use in connection with Gencaro or our other product candidates. Because patent applications can take many years to issue, there may be other currently pending applications that may later result in issued patents that are infringed by rNAPc2, Gencaro or our other product candidates. Moreover, a license may not be available to us on commercially reasonable terms, or at all.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we are infringing on its technology, then our business and results of operations could be harmed by a number of factors, including:

- infringement and other intellectual property claims, even if without merit, are expensive and time-consuming to litigate and can divert management's attention from our core business;
- monetary damage awards for past infringement can be substantial;
- a court may prohibit us from selling or licensing product candidates unless the patent holder chooses to license the patent to us; and
- if a license is available from a patent holder, we may have to pay substantial royalties.

We may also be forced to bring an infringement action if we believe that a competitor is infringing our protected intellectual property. Any such litigation will be costly, time-consuming and divert management's attention, and the outcome of any such litigation may not be favorable to us.

***Our intellectual property rights may not preclude competitors from developing competing products and our business may suffer.***

Our competitive success will depend, in part, on our ability to obtain and maintain patent protection for our inventions, technologies and discoveries, including intellectual property that we license. The patent positions of biotechnology companies involve complex legal and factual questions, and we cannot be certain that our patents and licenses will successfully preclude others from using our technology. Consequently, we cannot be certain that any of our patents will provide significant market protection or will not be circumvented or challenged and found to be unenforceable or invalid. In some cases, patent applications in the United States and certain other jurisdictions are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention, in opposition proceedings in a foreign patent office, or in a post-grant challenge proceeding such as an *ex parte* reexamination or *inter partes* review at the U.S. Patent and Trademark Office, any of which could result in substantial cost to us, even if the eventual outcome is favorable. There can be no assurance that a court of competent jurisdiction would hold any claims in any issued patent to be valid. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using such technology.

We own the clinical development program of rNAPc2, including Phase 2 clinical trials. If rNAPc2 is successfully developed, we believe it will have intellectual property protection, including 12 years of market exclusivity as an innovative biologic product under FDA law in the United States, 10 years data protection exclusivity in the EU, and potentially patent protection in addition to this. However, another competitor could develop a compound with similar biological properties to rNAPc2 that may not be barred by our exclusivity. We have also filed a provisional patent application for rNAPc2 and its use for COVID-19 disease, but there is no assurance that this provisional application will ultimately result in an issued patent.

Regardless of merit, the listing of patents in the FDA Orange Book for Gencaro may be challenged as being improperly listed. We may have to defend against such claims and possible associated antitrust issues. We could also incur substantial costs in seeking to enforce our proprietary rights against infringement.

While the composition of matter patents on the compound that comprises Gencaro have expired, we hold the intellectual property concerning the interaction of Gencaro with the polymorphisms of the beta-1 and alpha-2C receptors. We have obtained patents that claim methods involving Gencaro after a patient's receptor genotype has been determined. We anticipate that any NDA for Gencaro will request a label including a claim that efficacy varies based on receptor genotype and a recommendation in the prescribing information that prospective patients be tested for their receptor genotype. We believe that under applicable law, a generic bucindolol label would likely be required to include this recommendation as it pertains directly to the safe or efficacious use of the drug. Such a label may be considered as inducing infringement, carrying the same liability as direct infringement. If the label with the genotype information for Gencaro is not approved, or if generic labels are not required to copy the approved label, competitors could have an easier path to introduce competing products and our business may suffer. The approved label may not contain language covered by the patents, or we may be unsuccessful in enforcing them.

We may not be able to effectively protect our intellectual property rights in some foreign countries, as our patents are limited by jurisdiction and many countries do not offer the same level of legal protection for intellectual property as the United States.

We require our employees, consultants, business partners and members of our scientific advisory board to execute confidentiality agreements upon the commencement of employment, consulting or business relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions resulting from work performed for us, utilizing the property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law.

Third parties may breach these and other agreements with us regarding our intellectual property and we may not have adequate remedies for the breach. Third parties could also fail to take necessary steps to protect our licensed intellectual property, which could seriously harm our intellectual property position.

If we are not able to protect our proprietary technology, trade secrets and know-how, then our competitors may develop competing products. Any issued patent may not be sufficient to prevent others from competing with us. Further, we have trade secrets relating to rNAPc2 and Gencaro, and such trade secrets may become known or independently discovered. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, opposed, invalidated or circumvented, which could allow competitors to market similar products or limit the patent protection term of our product candidates. All of these factors may affect our competitive position.

***If the manufacture, use or sale of our products infringe on the intellectual property rights of others, we could face costly litigation, which could cause us to pay substantial damages or licensing fees and limit our ability to sell some or all of our products.***

Extensive litigation regarding patents and other intellectual property rights has been common in the biopharmaceutical industry. Litigation may be necessary to assert infringement claims, enforce patent rights, protect trade secrets or know-how and determine the enforceability, scope and validity of certain proprietary rights. Litigation may even be necessary to defend disputes of inventorship or ownership of proprietary rights. The defense and prosecution of intellectual property lawsuits, U.S. Patent and Trademark Office interference proceedings, and related legal and administrative proceedings (e.g., a reexamination, *inter partes* review, or post-grant review) in the United States and internationally involve complex legal and factual questions. As a result, such proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

Regardless of merit or outcome, our involvement in any litigation, interference or other administrative proceedings could cause us to incur substantial expense and could significantly divert the efforts of our technical and management personnel. Any public announcements related to litigation or interference proceedings initiated or threatened against us could cause our stock price to decline. Adverse outcomes in patent litigation may potentially subject us to antitrust litigation which, regardless of the outcome, would adversely affect our business. An adverse determination may subject us to the loss of our proprietary position or to significant liabilities, or require us to seek licenses that may include substantial cost and ongoing royalties. Licenses may not be available from third parties, or may not be obtainable on satisfactory terms. An adverse determination or a failure to obtain necessary licenses may restrict or prevent us from manufacturing and selling our products, if any. These outcomes could materially harm our business, financial condition and results of operations.

**Risks Related to Ownership of our Common Stock and Stock Price Volatility**

***Our stock price has been and is expected to be volatile.***

Our common stock has in the past been and in the future could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the regulatory status of rNAPc2, Gencaro and the genetic test, and whether and when they are approved for sale, if at all, and the labeling or other conditions of use imposed by the FDA;
- our ability to secure additional funding or complete a strategic transaction or to complete development of and commercialize rNAPc2 or Gencaro;
- progress of any future clinical trials for rNAPc2, Gencaro or our other product candidate, including enrollment and any data that may become available;
- the results of our future clinical trials and any future NDAs of our current and future product candidates;
- the entry into, or termination of, key agreements, including key strategic alliance agreements;
- the results and timing of regulatory reviews relating to our product candidates;
- failure of any of our product candidates, if approved, to achieve commercial success;
- general and industry-specific economic conditions that may affect our research and development expenditures;
- the results of clinical trials conducted by others on drugs that would compete with our product candidates;
- issues in manufacturing our product candidates or any approved products;
- the initiation of or material developments in or the conclusion of litigation to enforce or defend any of our intellectual property rights;
- the loss of key employees;
- the introduction of technological innovations or new commercial products by our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- future sales of our common stock;
- changes in the structure of health care payment systems;
- period-to-period fluctuations in our financial results; and
- our ability to retain the listing of our common stock on the Nasdaq Capital Market.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies, including as a result of the ongoing COVID-19 pandemic. These broad market fluctuations may also adversely affect the trading price of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

***Future sales or the possibility of future sales of our common stock may depress the market price of our common stock.***

Sales in the public market of substantial amounts of our common stock could depress prevailing market prices of our common stock. As of September 30, 2021, approximately 14.4 million shares of common stock were outstanding, and all of these shares are freely transferable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, except for shares held by our directors, officers and other affiliates and unregistered shares held by non-affiliates. The sale of these additional shares, or the perception that such sales may occur, could depress the market price of our common stock.

As of September 30, 2021, approximately 133,000 shares of our common stock were issuable upon the exercise of outstanding warrants. Once a warrant is exercised, if the shares of our common stock issued upon the exercise of any such warrant are not available for sale in the open market without further registration under the Securities Act, then the holder can arrange for the resale of shares either by invoking any applicable registration rights, causing the shares to be registered under the Securities Act and thus freely transferable, or by relying on an exemption to the Securities Act. For instance, in July 2015, we filed a registration statement on Form S-3 which registered for resale an aggregate of 0.1 million shares of our common stock issuable upon exercise of outstanding warrants. If these registration rights, or similar registration rights that may apply to securities we may issue in the future, are exercised, it could result in additional sales of our common stock in the market, which may have an adverse effect on our stock price.

As of September 30, 2021, there were approximately 641,000 shares of our common stock which may be issued upon the exercise of outstanding stock options, and we anticipate that we will continue to issue stock option awards to our employees and consultants in the fiscal year ended December 31, 2021 and thereafter. If and when these options are exercised, such shares will be available for sale in the open market without further registration under the Securities Act. The existence of these outstanding options may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options, and the prompt resale of shares of our common stock received, may also result in downward pressure on the price of our common stock.

In the absence of a significant strategic transaction, we will need to raise significant additional capital to finance the research, development and commercialization of rNAPc2, Gencaro and our other product candidate. If future securities offerings occur, they would dilute our current stockholders' equity interests and could reduce the market price of our common stock.

***We do not expect to pay cash dividends, and accordingly, stockholders must rely on stock appreciation for any return on their investment.***

We anticipate that we will retain our earnings, if any, for future growth and therefore do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

***We have implemented anti-takeover provisions that could discourage, prevent or delay a takeover, even if the acquisition would be beneficial to our stockholders.***

Provisions of our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions:

- establish a classified board of directors so that not all members of our board may be elected at one time;
- authorize the issuance of up to approximately 5 million additional shares of preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt;
- limit who may call a special meeting of stockholders;
- prohibit stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders; and
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at a stockholder meeting.

Specifically, our certificate of incorporation provides that all stockholder action must be effected at a duly called meeting and not by a written consent. The bylaws provide, however, that our stockholders may call a special meeting of stockholders only upon a request of stockholders owning at least 50% of our outstanding common stock. These provisions of our certificate of incorporation and bylaws could discourage potential acquisition proposals and could delay or prevent a change in control. We designed these provisions to reduce our vulnerability to unsolicited acquisition proposals and to discourage certain tactics that may be used in proxy fights. These provisions, however, could also have the effect of discouraging others from making tender offers for our shares. As a consequence, they also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

We are permitted to issue shares of our preferred stock without stockholder approval upon such terms as our board of directors determines. Therefore, the rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of our preferred stock that may be issued in the future. In addition, the issuance of preferred stock could have a dilutive effect on the holdings of our current stockholders.

We are subject to the Delaware anti-takeover laws regulating corporate takeovers. These anti-takeover laws prevent a Delaware corporation from engaging in a merger or sale of more than 10% of its assets with any stockholder, including all affiliates and associates of the stockholder, who owns 15% or more of the corporation's outstanding voting stock, for three years following the date that the stockholder acquired 15% or more of the corporation's stock unless:

- the board of directors approved the transaction where the stockholder acquired 15% or more of the corporation's stock;
- after the transaction in which the stockholder acquired 15% or more of the corporation's stock, the stockholder owned at least 85% of the corporation's outstanding voting stock, excluding shares owned by directors, officers and employee stock plans in which employee participants do not have the right to determine confidentially whether shares held under the plan will be tendered in a tender or exchange offer; or
- on or after this date, the merger or sale is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock that is not owned by the stockholder.

The provisions of our governing documents and current Delaware law may, collectively:

- lengthen the time required for a person or entity to acquire control of us through a proxy contest for the election of a majority of our board of directors;
- discourage bids for our common stock at a premium over market price; and
- generally deter efforts to obtain control of us.

**ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS**

Not applicable.

**ITEM 3. DEFAULTS UPON SENIOR SECURITIES**

Not applicable.

**ITEM 4. MINE SAFETY DISCLOSURES**

Not applicable.

**ITEM 5. OTHER INFORMATION**

**2021 Corporate Performance Goals**

On October 29, 2021, the Compensation Committee approved corporate performance goals for the fiscal year ending December 31, 2021. The corporate performance goals, which may be updated at the Board's discretion during 2021, include:

- goals related to executing our development plan for rNAPc2 (AB201), our clinical product candidate for the treatment of patients with COVID-19;
- goals related to further defining our development plan for Gencaro, our clinical product candidate for the treatment of atrial fibrillation; and
- finance and corporate compliance goals.

**ITEM 6. EXHIBITS**

**EXHIBIT INDEX**

The following documents are filed as part of this quarterly report on Form 10-Q. The Company will furnish a copy of any exhibit listed to requesting stockholders upon payment of the Company's reasonable expenses in furnishing those materials.

| Exhibit No. | Description | Incorporated by Reference (1) | | | Filed Herewith |
|---|---|---|---|---|---|
| | | Form | Filing Date | Number | |
| 3.1 | Amended and Restated Certificate of Incorporation of the Registrant, as amended. | 10-K | 3/27/2009 | 3.1 | |
| 3.1(a) | Certificate of Amendment to Restated Certificate of Incorporation. | 8-K | 3/5/2013 | 5.1 | |
| 3.1(b) | Certificate of Amendment to Restated Certificate of Incorporation. | 8-K | 9/3/2015 | 3.1 | |
| 3.1(c) | Certificate of Amendment to Restated Certificate of Incorporation. | 8-K | 4/3/2019 | 3.1 | |
| 3.2 | Amended and Restated Bylaws of the Registrant, as amended. | 8-K | 6/28/2021 | 3.1 | |
| 4.1 | Reference is made to Exhibits 3.1, 3.1(a), 3.1(b) and 3.2 | | | | |
| 4.2 | Form of Common Stock Certificate. | 10-Q | 5/8/2019 | 4.2 | |
| 31.1 | Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 31.2 | Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 32.1 | Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. sec. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 101.INS | Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document | | | | X |
| 101.SCH | Inline XBRL Taxonomy Extension Schema Document (filed electronically herewith) | | | | X |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document (filed electronically herewith) | | | | X |
| 101.LAB | Inline XBRL Taxonomy Extension Label Linkbase Document (filed electronically herewith) | | | | X |
| 101.PRE | Inline XBRL Taxonomy Extension Presentation Linkbase Document (filed electronically herewith) | | | | X |

| Exhibit No. | Description | Incorporated by Reference (1) | | | Filed Herewith |
|---|---|---|---|---|---|
| | | Form | Filing Date | Number | |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document (filed electronically herewith) | | | | X |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document). | | | | |

**(1)** The SEC file number for all items incorporated by reference herein from reports on Forms 10-K, 10-Q and 8-K is 000-22873.

**SIGNATURE**

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

ARCA biopharma, Inc. (Registrant)

By: /s/ C. Jeffrey Dekker

**C. Jeffrey Dekker**
**Chief Financial Officer**
**(Principal Financial and Accounting Officer)**

Dated: November 2, 2021

**Exhibit 31.1**

## CERTIFICATION

I, Michael R. Bristow, certify that:

1. I have reviewed this quarterly report on Form 10-Q of ARCA biopharma, Inc.;

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

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

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

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

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: November 2, 2021

/s/ Michael R. Bristow

**Michael R. Bristow**
*President and Chief Executive Officer*
*(Principal Executive Officer)*

**Exhibit 31.2**

## CERTIFICATION

I, C. Jeffrey Dekker, certify that:

1. I have reviewed this quarterly report on Form 10-Q of ARCA biopharma, Inc.;

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

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

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

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

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: November 2, 2021

/s/ C. Jeffrey Dekker

**C. Jeffrey Dekker**
*Chief Financial Officer*
*(Principal Financial and Accounting Officer)*

**Exhibit 32.1**

**ARCA BIOPHARMA, INC.**

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

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Michael R. Bristow, Chief Executive Officer of ARCA biopharma, Inc. (the "Company"), and C. Jeffrey Dekker, Chief Financial Officer of the Company, each hereby certifies that, to the best of his/her knowledge:

(1) The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2021, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report") fully complies with the requirements of section 13(a) or 15(d) of the Exchange Act; and

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

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

| /s/ Michael R. Bristow | /s/ C. Jeffrey Dekker |
|---|---|
| **Michael R. Bristow** | **C. Jeffrey Dekker** |
| *President and Chief Executive Officer* | *Chief Financial Officer* |
| *(Principal Executive Officer)* | *(Principal Financial and Accounting Officer)* |

A signed original of this written statement required by Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. § 1350, as adopted) has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request. This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of ARCA biopharma, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.