Adamas Pharmaceuticals Inc
Form 8-K
January 22, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **January 22, 2018**

Adamas Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-36399**	**42-1560076**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

1900 Powell Street, Suite 750 **Emeryville, CA**	**94608**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: **(510) 450-3500**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company x

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. x

Item 2.02. Results of Operations and Financial Condition.

On January 22, 2018, we expect to file with the Securities and Exchange Commission a Prospectus Supplement in which we will disclose that we had approximately $176.4 million in cash, cash equivalents and investments at December 31, 2017.

Item 8.01. Other Events.

On January 22, 2018, we provided an update to our risk factors, as last disclosed in our Quarterly Report on Form 10-Q for the three months ended September 30, 2017. These risk factors, as updated, read as follows:

RISK FACTORS

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition, results of operations, and future growth prospects. Our business could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained in our filings with the Securities and Exchange Commission, or SEC, including our condensed consolidated financial statements and related notes included therein.

Risks related to the commercialization of GOCOVRITM (amantadine) extended release capsules (formerly ADS-5102)

Our success depends heavily on successful commercialization of GOCOVRI, which received approval in August 2017 from the U.S. Food and Drug Administration, or FDA, for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications. To the extent GOCOVRI is not commercially successful, our business, financial condition and results of operations will be materially harmed.

We have invested and continue to invest a significant portion of our efforts and financial resources in the development, approval and now commercialization of GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications. The success of GOCOVRI will depend on numerous factors, including:

- our success in commercializing GOCOVRI, including the marketing, sales, and distribution of the product;
- successfully establishing and maintaining commercial manufacturing with third parties;

- acceptance of GOCOVRI by physicians, patients and the healthcare community;
- the acceptance of pricing and placement of GOCOVRI on payers formularies and the associated tiers;
- effectively competing with other approved or used medicines and future compounds in development;
- continued demonstration of an acceptable safety profile of GOCOVRI following approval; and
- obtaining, maintaining, enforcing, and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize GOCOVRI, which would materially harm our business.

GOCOVRI may fail to achieve the degree of market acceptance by physicians, patients, healthcare payers, and others in the medical community necessary for commercial success, negatively impacting our business.

GOCOVRI may fail to gain sufficient market acceptance by physicians, hospital administrators, patients, healthcare payers, and others in the healthcare community. The degree of market acceptance of GOCOVRI will depend on a number of factors, including:

- its efficacy, duration of response, and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the acceptability of the price of GOCOVRI;
- the willingness of physicians to change their current treatment practices;
- its convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our marketing, promotion, selling, and distribution support; and
- the availability of third-party insurance coverage or reimbursement.

The failure of GOCOVRI to achieve market acceptance would negatively impact our business.

If we are unable to effectively market, promote, sell, and distribute GOCOVRI and to retain experienced commercial personnel, our business will be substantially harmed.

We currently have limited experience in marketing, selling and distributing pharmaceutical products. With respect to GOCOVRI in particular, it is a newly marketed drug and is the first and only drug approved by the FDA for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications. Therefore, none of the members of our recently hired commercial team, including our sales force, has ever promoted GOCOVRI prior to its launch, and we have only recently established our distribution and reimbursement capabilities, all of which will be necessary to successfully commercialize GOCOVRI. As a result, we will be

required to expend significant time and resources to market, sell, and distribute GOCOVRI to neurologists and movement disorder specialists in a credible, persuasive, and compliant manner consistent with applicable laws. There is no guarantee that the strategies, tactics and marketing messages, or the distribution and reimbursement capabilities, that we have developed will be successful. Specifically, for distribution of GOCOVRI, we are heavily dependent on third-party logistics, pharmacy and distribution partners. If they are unable to perform effectively or if they do not provide efficient distribution of the medicine to patients, our business will suffer. Also, if we are unable to effectively market and sell GOCOVRI for any reason, including our ineffective training of our sales force or equipping them with ineffective materials, including medical and sales literature to help them inform and educate potential customers about the benefits and risks of GOCOVRI and its proper administration, our efforts to successfully commercialize could be put in jeopardy.

Failure to successfully obtain coverage and reimbursement for GOCOVRI in the United States, or the availability of coverage and reimbursement only at limited levels, would diminish our ability to generate product revenue.

Our ability to commercialize GOCOVRI successfully in the United States will depend in part on the extent to which coverage and reimbursement for GOCOVRI becomes available from third-party payers, including government health administration authorities, such as those that administer the Medicare and Medicaid programs, and private health insurers. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payers to

reimburse all or part of the costs associated with their prescription drugs. Coverage and reimbursement discussions are currently ongoing with payers. Coverage and adequate reimbursement from both governmental healthcare programs, such as Medicare and Medicaid, and commercial payers are critical to GOCOVRI s commercial success. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or cheaper therapeutic alternatives are already available or subsequently become available. For example, although no payer has done so to date, a payer may determine to require patients to use immediate release amantadine for dyskinesia (even though it is not approved for that indication) prior to receiving reimbursement for GOCOVRI.

Coverage and reimbursement may not be available for GOCOVRI. Even if we obtain coverage for GOCOVRI, the resulting reimbursement rates might not be adequate or may require co-payments or co-insurance payments that patients find unacceptably high. Coverage and reimbursement determinations by third-party payers will impact the demand for GOCOVRI and therefore our revenues. Patients may choose not to use GOCOVRI if coverage is not provided or reimbursement is inadequate to cover a significant portion of its cost. If coverage and reimbursement are not available or are available only to limited levels, we may not be able to successfully commercialize GOCOVRI.

As with any newly approved medicine for a particular indication, there may be significant delays in obtaining final coverage and reimbursement decisions for GOCOVRI. Third-party payers are increasingly challenging the price and reviewing the cost-effectiveness of medical drug products, in addition to questioning their safety and efficacy. Coverage and reimbursement decisions for GOCOVRI by third-party payers are generally subject to change and may not be permanent.

Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs, such as the federal 340B Drug Pricing Program, or by private third-party payers and could also be adversely affected by any future relaxation of laws that currently restrict imports of products from countries where they may be sold at lower prices than in the United States. In the United States, private third-party payers often rely upon Medicare coverage and reimbursement policies and payment limitations in setting their own coverage and reimbursement policies.

Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private third-party payers for GOCOVRI could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We face substantial competition in the commercialization of GOCOVRI.

The commercialization of new pharmaceutical products is highly competitive, and we face substantial competition with respect to GOCOVRI. For example, although GOCOVRI is the first and only FDA-approved medicine for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, we may face competition from various drugs approved for the treatment of Parkinson s disease, such as Azilect (Teva Pharmaceuticals Industries, Ltd.), Requip XL (GlaxoSmithKline plc), Mirapex ER (Boehringer Ingelheim Pharmaceuticals Inc.), Neupro Patch (UCB SA/NV), Sinemet (Merck & Co., Inc.), Parcopa (Schwartz Pharma, Mylan and others), Rytary (Impax), Duopa (AbbVie), Xadago (Newron Pharmaceuticals S.p.A.) and immediate release amantadine. Other products in late stage development for Parkinson s disease includes product candidates from Acorda, Mitsubishi Tanabe, Bial-Portela CSA, Genervon Biopharmaceuticals, and Pharma Two B. GOCOVRI may also face competition from drugs currently in development for dyskinesia in Parkinson s disease or for Parkinson s disease from a number of pharmaceutical companies, such as Novartis, Osmotica Pharmaceuticals Corp., Avanir Pharmaceuticals, Neurolixis, Amarantus BioScience, Addex Pharma, and Neurim Pharmaceuticals Ltd. In addition, GOCOVRI will face competition from the medical strategies historically used by physicians to manage dyskinesia, such as levodopa dose fractionation.

Many of our competitors, including a number of large pharmaceutical companies that compete directly with us, have significantly greater financial resources and expertise commercializing approved products than we do. Also, many of our competitors are large pharmaceutical companies that will have a greater ability to reduce prices for their competing drugs in an effort to gain market share and undermine the value proposition that we might otherwise be able to offer to payers.

Also, GOCOVRI may potentially face competition from other extended release versions of amantadine that may be in development. For example, other extended release versions of amantadine may be in development for the treatment of Parkinson s disease.

If we are unable to maintain orphan exclusivity for GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, our business may be substantially harmed.

Under the Orphan Drug Act, the FDA may designate a drug product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. Generally, if a drug product with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the drug product is entitled to a period of marketing exclusivity, which may preclude the FDA from approving another marketing application for the same drug product for the same therapeutic indication. The applicable period of exclusivity is up to seven years in the United States. GOCOVRI received orphan designation for the treatment of levodopa-induced dyskinesia in 2015. When it was approved for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, GOCOVRI earned seven years of orphan drug exclusivity. The FDA has recognized GOCOVRI s orphan drug exclusivity by letter to us on its Orphan Drug Designation and Approvals database listing and the *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book.

Although we have obtained marketing approval for GOCOVRI for the treatment of dyskinesia, the FDA could still subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer or more effective or makes a major contribution to patient care, or if we are unable to assure that sufficient quantities of medicine are available to meet patient needs. If we are unable to maintain orphan drug exclusivity for GOCOVRI for the treatment of dyskinesia, our business would be substantially harmed.

If manufacturers obtain approval for generic versions of GOCOVRI, or of products with which we compete, our business may suffer.

Under the U.S. Food, Drug and Cosmetic Act, or FDCA, the FDA can approve an Abbreviated New Drug Application, or ANDA, for a generic version of a branded drug without the ANDA applicant undertaking the clinical testing necessary to obtain approval to market a new drug. Generally, in place of such clinical studies, an ANDA applicant usually needs only to submit data demonstrating that its product has the same active ingredient(s), strength, dosage form, route of administration and that it is bioequivalent to the branded product.

The FDCA requires that an applicant for approval of a generic form of a branded drug certify either that its generic product does not infringe any of the patents listed by the owner of the branded drug in the Orange Book or that those patents are not enforceable. This process is known as a paragraph IV challenge. Upon notice of a paragraph IV challenge, a patent owner has 45 days to bring a patent infringement suit in federal district court against the company seeking ANDA approval of a product covered by one of the owner s patents. If this type of suit is commenced, the FDCA provides a 30-month stay on the FDA s approval of the competitor s application. If the litigation is resolved in favor of the ANDA applicant or the challenged patent expires during the 30-month stay period, the stay is lifted and the FDA may thereafter approve the application based on the standards for approval of ANDAs. Once an ANDA is approved by the FDA, the generic manufacturer may market and sell the generic form of the branded drug in competition with the branded medicine.

The ANDA process can result in generic competition if the patents at issue are not upheld or if the generic competitor is found not to infringe the owner s patents. If this were to occur with respect to GOCOVRI or products with which it competes, our business would be materially harmed. Furthermore, even if ultimately successful, ANDA litigation can take several years and is generally time-consuming and costly. Such litigation has been commenced by Forest Laboratories Holdings Limited, or Forest, an indirect wholly-owned subsidiary of Allergan plc, referred to collectively with Forest as Allergan, and us to enforce certain patents related to Namenda XR® and Namzaric®. Further information about this litigation can be found in our Quarterly Report on Form 10-Q for the three months ended September 30, 2017 filed with the SEC. Although the appeal process is not fully concluded, based on adverse trial and appellate court rulings to date with respect to Namenda XR, we do not expect to receive royalties on net sales of Namenda XR due to the potential entry of generic versions Namenda XR. The pending ANDA litigation with respect to Namzaric is at a very early stage.

There is an ongoing open label safety study with GOCOVRI in Parkinson s disease patients with dyskinesia. New safety findings regarding GOCOVRI from this study could harm our business.

There is an ongoing safety study with GOCOVRI. If any new safety concerns emerge from this ongoing clinical study, we may:

- have the product removed from the market;
- be subject to additional post-marketing testing requirements; or
- be subject to restrictions on how the product is distributed, marketed, or used.

Any of these unforeseen events could impair our ability to commercialize GOCOVRI and harm our business and results of operations.

Unforeseen safety issues could emerge with GOCOVRI that could require us to change the prescribing information to add warnings, limit use of the product, and/or result in litigation. Any of these events could have a negative impact on our business.

Discovery of unforeseen safety problems or increased focus on a known problem could impact our ability to commercialize GOCOVRI and could result in restrictions on its permissible uses, including withdrawal of the medicine from the market.

If we or others identify additional undesirable side effects caused by GOCOVRI after approval:

- regulatory authorities may require the addition of labeling statements, specific warnings, contraindications, or field alerts to physicians and pharmacies;

- regulatory authorities may withdraw their approval of the product and require us to take our approved drugs off the market;

- we may be required to change the way the product is administered, conduct additional clinical trials, change the labeling of the product, or implement a Risk Evaluation and Mitigation Strategy, or REMS;

- we may have limitations on how we promote our drugs;

- third-party payers may limit coverage or reimbursement for GOCOVRI;

- sales of GOCOVRI may decrease significantly;

- we may be subject to litigation or product liability claims; and

- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of GOCOVRI and could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from its sale.

Further, GOCOVRI may also be affected by the safety and tolerability of its parent drug or drugs with similar mechanisms of action. Although amantadine, which is a component of GOCOVRI, has been used in patients for many years, newly observed toxicities or worsening of known toxicities in preclinical studies or in subjects in clinical studies receiving amantadine, or reconsideration of known toxicities of compounds in the setting of new indications, could result in increased regulatory scrutiny of our products and product candidates.

In addition, problems with approved products marketed by third parties that utilize the same therapeutic target or that belong to the same therapeutic class as amantadine could adversely affect the commercialization of GOCOVRI.

If a safety issue emerges post-approval, we may become subject to costly product liability litigation by our customers, their patients or payers. Product liability claims could divert management s attention from our core business, be expensive to defend, and result in sizable damage awards against us that may not be covered by insurance. If we cannot successfully defend ourselves against claims that GOCOVRI caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- the inability to commercialize any products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of patients from clinical studies or cancellation of studies;
- significant costs to defend the related litigation;
- substantial monetary awards to patients; and
- loss of revenue.

We currently hold $10.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to obtain insurance coverage at a reasonable cost or in amounts adequate to satisfy any liability or associated costs that may arise in the future. These events could harm our business and results of operations and cause our stock price to decline.

The marketing and promotion of GOCOVRI will be limited to the approved indication for use and the information and clinical data included in or consistent with the approved prescribing information. If we want to expand the marketing and promotion of GOCOVRI beyond the approved indication or with information not consistent with the approved prescribing information, we will need to obtain additional regulatory approvals, which may not be granted.

With the August 2017 approval of GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, we are permitted to market or promote it only for the treatment of dyskinesia and not for other uses. We are developing GOCOVRI for at least one additional indication, treatment of walking impairment in patients with multiple sclerosis, and potentially others. In order to market and promote GOCOVRI for these additional indications, we will need to conduct additional clinical trials that will likely be time-consuming and expensive to obtain regulatory approval for such uses. Additionally, our current marketing and promotional efforts will be limited to the use of information included in or deemed to be consistent with the approved prescribing information for GOCOVRI for the treatment of dyskinesia, including the clinical data and results reflected in the prescribing information. To use information not consistent with the approved prescribing information will require additional regulatory approvals.

If we are found to have improperly promoted unapproved uses of GOCOVRI, or if physicians misuse it, we may be subject to restrictions on the sale or marketing of GOCOVRI and significant fines, penalties, sanctions and product liability claims, and our image and reputation within the industry and marketplace could be harmed.

The FDA and other regulatory agencies, including regulatory authorities outside the United States, strictly regulate the marketing and promotional claims that are made about drug products, such as GOCOVRI. In particular, promotion for a product must be consistent with its labeling approved by the FDA or by regulatory agencies in other countries. For example, in the case of GOCOVRI, for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, we cannot prevent physicians from prescribing GOCOVRI for indications or uses that are inconsistent with the approved label. If, however, we are found to have promoted such unapproved uses prior to the FDA s approval for an additional indication, we may, among other consequences, receive untitled or warning letters and become subject to significant liability, which would materially harm our business. Both the U.S. federal government and foreign regulatory authorities have levied significant civil and criminal fines against companies and individuals for alleged improper promotion and have entered into settlement agreements with pharmaceutical companies to limit inappropriate promotional activities. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management s attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged.

Physicians prescribing of our products for unapproved uses may also subject us to product liability claims, to the extent such uses lead to adverse events, side effects, or injury. Product liability claims could divert management s attention from our core business, be expensive to defend, and result in sizable damage awards against us that may not be covered by insurance. Furthermore, the use of our products for indications other than those approved by the FDA or regulatory authorities outside the United States may not effectively treat such conditions, which could harm our reputation in the marketplace among physicians and patients. Any of these events could harm our business and results of operations and cause our stock price to decline.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have a material adverse effect on our business, results of operations and financial condition.

We will participate in the Medicaid Drug Rebate Program, as administered by the Centers for Medicare and Medicaid Services, or CMS, and other federal and state government pricing programs in the United States, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payers in connection with drugs that are dispensed to beneficiaries/recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate/discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. Responding to current and future changes may increase our costs, and the complexity of compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, there can be no assurance that we will be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have a material adverse effect on our business, results of operations and financial condition.

In addition, the Office of Inspector General of the Department of Health and Human Services and other Congressional enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price, or AMP, and best price, or BP, for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payers. For example, failure to submit monthly/quarterly AMP and BP data on a timely basis could result in a civil monetary penalty of $18,107 per day for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In addition, in the event that CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

GOCOVRI is complex to manufacture, and manufacturing disruptions may occur that could cause us to experience disruptions in the supply of GOCOVRI.

GOCOVRI is an extended release version of amantadine. The manufacture of extended release versions of drugs is more complex than the manufacture of the immediate release versions of drugs. Notwithstanding the fact that we have validated our process, manufacturing disruptions may occur. Such problems may prevent the production of lots that meet the specifications required for sale of the product and may be difficult and expensive to resolve. If any such issues were to arise with respect to GOCOVRI or our future product candidates, our business, financial results, or stock price could be adversely affected.

Risks related to our product candidates in clinical development

Our success depends on the timely clinical development, approval and successful commercialization of our product candidates. If we are unable to do any of these with our product candidates or if we experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources into the development and potential commercialization of our product candidates, including ADS-5102 for the treatment of walking impairment in patients with multiple sclerosis, and potentially other indications, as well as ADS-4101 for the treatment of partial onset seizures in epilepsy. Our ability to generate product revenue will depend heavily on the successful development, regulatory approval, and commercialization of our other product candidates. The success of our product candidates will depend on numerous factors, including:

- successfully completing the development program for our product candidates in a timely manner;
- receiving marketing approval for our product candidates from the FDA in a timely manner;
- successfully establishing and maintaining commercial manufacturing with third parties;

- commercializing our product candidates, if approved, including marketing, sales, and distribution of the product independently or in partnership with another company;

- acceptance by the medical community and patients of the approved product;

- the pricing and placement of our product candidates on payers formulary tiers and the reimbursement rates established for the approved products;

- effectively competing with other approved or used medicines and future compounds in development;

- continued demonstration of an acceptable safety profile of the approved products following approval; and

- obtaining, maintaining, enforcing, and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

We will face risks in the development of ADS-5102 (GOCOVRI) for additional indications, ADS-4101 and other product candidates.

There are risks associated with pursuing clinical trials in other indications for ADS-5102 (GOCOVRI), ADS-4101 and other product candidates, as we may experience numerous unforeseen events during, or as a result of clinical studies that could harm our ability to commercialize such products and candidates or to receive regulatory approval, including that:

- clinical studies may produce negative or inconclusive results or raise significant safety concerns, and we may decide, or regulators may require us, to conduct additional clinical studies or abandon product development programs;

- even if clinical studies demonstrate statistically significant efficacy and acceptable safety, the FDA or similar authorities outside the United States may not consider the results of our studies to be sufficient for approval;

- our clinical sites and clinical investigators may fail to comply with, or inconsistently apply, the trial protocols, regulatory requirements including Good Clinical Practices, contractual obligations, and the rating assessments;

- our third-party vendors, including our Contract Research Organizations, or CROs, and contract manufacturing organizations, or CMOs, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we might have to suspend or terminate clinical studies for various reasons, including a finding that our product candidates have unanticipated serious side effects or other unexpected characteristics or that the patients are being exposed to unacceptable health risks;

- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;

- the supply or quality of ADS-5102, ADS-4101, or other materials necessary to conduct clinical studies may be insufficient or inadequate; and

- our new product discovery or research program may not be successful or warrant clinical development.

With respect to the development of additional indications for GOCOVRI, although the safety profile of amantadine, the active pharmaceutical ingredient in GOCOVRI, is already characterized in the approved label for amantadine (i.e., Symmetrel®) and in the GOCOVRI clinical trial data in the dyskinesia population, there can be no assurance that our clinical development program for ADS-5102 (GOCOVRI) for multiple sclerosis walking impairment or future studies in other indications will not reveal additional safety or tolerability issues that could lead to changes in the GOCOVRI prescribing information. In such an event, our ability to commercialize GOCOVRI for dyskinesia and/or expand our business could be compromised.

If we are forced to delay or abandon development of our product candidates, our business, results of operations, and financial condition will be materially and adversely harmed.

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

Because we have limited financial and managerial resources, we have chosen to focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our investment in current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

Failure to gain approval of or successfully commercialize our product candidates in the United States could substantially harm our business.

Our product candidates will face the same or similar challenges in obtaining FDA approval and in commercialization as GOCOVRI, as outlined above, including but not limited to market acceptance by physicians and patients and coverage and reimbursement by third party payers.

Failure to obtain regulatory approvals in foreign jurisdictions would prevent us from marketing our products internationally.

We may decide to seek marketing authorizations to commercialize GOCOVRI, ADS-4101, and other future product candidates outside of the United States. To market our future products in the European Union, or EU, and many other foreign jurisdictions, we must obtain separate regulatory approvals. Specifically, in the EU, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

Before granting an MA, the European Medicines Agency, or EMA, or the competent authorities of the member states of the EU make an assessment of the risk-benefit balance of the product on the basis of a Common Technical Document including, among other information, scientific criteria concerning its quality, safety, and efficacy.

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states both before and after grant of the manufacturing and Marketing Authorizations. This includes control of compliance with current good manufacturing practices, or cGMP, rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third-party manufacturers are required to ensure that all of our processes, methods, and equipment are compliant with cGMP. Failure by us or by any of our third-party partners, including suppliers, manufacturers, and distributors, to comply with EU laws and the related national laws of individual EU member states governing the conduct of

clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant Marketing Authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

We have had limited interactions with foreign regulatory authorities. The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from and be longer than that required to obtain FDA approval. Clinical studies conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval as well as additional, different risks.

There is no assurance that we will be able to obtain marketing authorizations in foreign countries on a timely basis, if at all. We may not be able to file for foreign regulatory approvals, and even if we file we may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain non-U.S. regulatory approval to market our product candidates in other countries, we may not be able to achieve the financial results we project and our stock price could decline.

Risks related to our reliance on third parties

We rely on third-party contract manufacturing organizations to manufacture, serialize and supply GOCOVRI and our product candidates. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers and qualify them. We may also face delays in the development, commercialization, and supply of GOCOVRI or our product candidates.

We currently have limited experience in, and we do not own facilities for, clinical and commercial manufacturing of GOCOVRI or our product candidates, and we rely upon third-party contract manufacturing organizations to manufacture, serialize and supply drug product for our clinical studies and to meet potential commercial demand. The manufacture of pharmaceutical products in compliance with the FDA s cGMP requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements, and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our commercial supply of GOCOVRI or product candidates in our clinical trials could be jeopardized. Any delay or interruption in the supply of clinical study materials or commercial product could cause delays in our clinical programs, harm our ability to gain approval from regulatory authorities, and potentially disrupt patient access to our approved products. These events would substantially harm our business, reputation and stock price.

All third-party manufacturers of our products, product candidates and ingredients thereof must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance, and the maintenance of records and documentation. Manufacturers of our products and product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging, or testing of products. We have little control over our manufacturers compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products or product candidates and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals, commercialization or supply of our products or product candidates, entail higher costs, impair our reputation, and potentially disrupt patient access or our approved products.

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We rely on a single source third-party contract manufacturing organization for the manufacture and supply of our drug substances for GOCOVRI and our other product candidates.

We currently rely on single source suppliers for our drug substances for GOCOVRI and our other product candidates. We continue to seek additional long-term supply agreements with suppliers and supplier qualifications. A failure of our single source manufacturer or drug substance supplier or our failure to qualify at least one other manufacturer organization on a timely basis and validate the manufacturing process employed at that manufacturer or supplier could delay or harm commercialization of GOCOVRI or our product candidates. Although we believe alternative sources of supply exist, the number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange and negotiate acceptable long-term contracts and obtain regulatory approvals and qualifications, which would adversely affect our business. New suppliers of any product candidate would be required to be qualified under applicable regulatory requirements, including demonstration of bioequivalence of the product made at the new supplier, and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing the product candidate. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs, which may be passed on to us. Qualifying and negotiating long-term contracts with manufacturers and providers of packaging services is a lengthy process. If at any time, one or more of our qualified contract manufacturing organizations were not able to manufacture our drug substance or drug product or provide the requisite services, our business and financial condition would be materially adversely affected.

In our existing or any future potential collaborations or partnerships, we will likely not be able to control all aspects of the development and commercialization of our products or product candidates. This lack of control could subject us to additional risks that could harm our business.

Collaborations or license agreements involving our current or future products are subject to numerous risks, which may include that:

- partners have significant discretion in determining the efforts and resources that they will apply to collaborations;

- partners may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical study results, changes in their strategic focus due to the acquisition of competitive products, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities;

- partners may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study, abandon a product candidate, repeat or conduct new clinical studies, or require a new formulation of a product candidate for clinical testing;

- partners could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;

- a partner with marketing, manufacturing, and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;

- we could grant exclusive rights to our partners that would prevent us from collaborating with others;

- Allergan and future partners may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

- Allergan and future partners may not aggressively or adequately pursue litigation against ANDA filers or may settle such litigation on unfavorable terms, and as Allergan substantially controls the current ANDA litigation and terms of settlement and has different economic interests than ours, Allergan may grant licenses to generic manufacturers that permit them to make and sell generic versions of Namenda XR® and Namzaric®, which would negatively impact any royalties we may receive under our license with Allergan;

- disputes may arise between us and a partner that causes the delay or termination of the research, development, or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;

- agreements may be terminated, sometimes at-will, without penalty, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;

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

- a partner s sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of these trials.

We do not independently conduct clinical studies of our product candidates. Instead, we rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities, but does not relieve us of our responsibilities. For example, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practice, for conducting, recording, and reporting the results of clinical studies to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of patients in clinical studies are protected, even though we are not in control of these processes. These third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical studies in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also rely on other third parties to store and distribute supplies for our clinical studies. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

Risks related to government regulation

The regulatory approval process is expensive, time consuming, and uncertain and may prevent us or our collaboration partners from obtaining approvals for the commercialization of some or all of our product candidates.

The research, development, manufacturing, quality control, labeling, approval, safety, effectiveness, storage, record keeping, reporting, selling, import, export, advertising, promotion, marketing, and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States, and by regulatory authorities in other countries, with different regulations from country to country. Neither we nor our collaboration partners are permitted to market our product candidates in the United States or other countries until we receive FDA approval of an NDA. In August 2017, GOCOVRI was FDA-approved for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications. The FDA will need to approve supplemental NDAs for GOCOVRI before we can market the drug for other indications, such as multiple sclerosis walking impairment.

To receive approval to commercialize any of our product candidates in the United States, we and our collaboration partners must demonstrate with substantial evidence from adequate and well-controlled clinical studies, and to the satisfaction of the FDA, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical studies can be interpreted in different ways. Even if we and our collaboration partners believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA. Administering any of our product candidates to humans may produce undesirable side effects, which could interrupt, delay, or cause suspension of clinical studies of our product candidates and result in the denial of approval of our product candidates for any or all targeted indications.

FDA approval of an NDA is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense we invest, failure can occur at any stage, and we could encounter problems that require us to repeat clinical studies, perform additional preclinical studies and clinical studies, or abandon development and commercialization of a product candidate altogether. The number of preclinical studies and clinical studies that will be required for FDA approval varies depending on, among other factors, the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. The FDA can delay, limit, or deny approval of a product candidate for many reasons, including, but not limited to:

- disagreement with the design or implementation of our clinical trials;
- failure of clinical trials to show the level of statistical significance or clinical meaningfulness needed for approval;
- failure to demonstrate that a product candidate is safe or effective;
- insufficient data from preclinical and clinical studies to support an application;

- a finding by an institutional review board, or IRB, Data Safety Monitoring Board, or DSMB, Data Monitoring Committee, or DMC, or the FDA that the clinical trial exposes subjects or patients to an unacceptable health risk;

- disapproval of our or our third-party manufacturer s processes or facilities; or

- changes to FDA s approval policies or regulations.

If any of our product candidates fails to demonstrate safety and efficacy in clinical studies or does not gain regulatory approval, our business and results of operations will be materially and adversely harmed.

If the FDA concludes that our product candidates do not satisfy the requirements for approval under the Section 505(b)(2) regulatory approval pathway, or if the requirements for approval under Section 505(b)(2) are not as we expect, the approval pathway for our products will likely take significantly longer, cost significantly more, and entail significantly greater complications and risks than anticipated, and in any case may not be successful. Similar obstacles may arise in other countries.

Similar to the approval pathway for GOCOVRI, we are developing our current and future product candidates, with the expectation that they will be eligible for approval through the Section 505(b)(2) regulatory pathway. Section 505(b)(2) of the FDCA allows an NDA to rely in part on the FDA s prior conclusions regarding the safety and effectiveness of an approved drug product, or reference listed drug, or RLD. Use of the Section 505(b)(2) regulatory pathway could reduce the time required for the development programs of our product candidates by, for example, potentially decreasing the amount of preclinical and/or clinical data specific to a product candidate that we would need to generate in order to obtain FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for product approval. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates, and the complications and risks associated with regulatory approval would likely substantially increase. Moreover, our inability to pursue the Section 505(b)(2) regulatory pathway may result in competitive products reaching the market more quickly than our product candidates, which would adversely impact our competitive position and prospects. Even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee that utilizing this pathway will ultimately lead to faster product development or earlier approval for any product candidate that we may attempt to develop and commercialize.

An NDA submitted through the Section 505(b)(2) regulatory pathway for a drug product with an active moiety that has been previously approved in another product (e.g., amantadine) may be entitled to three years of regulatory exclusivity if the NDA contains data from clinical investigations (other than bioavailability or bioequivalence studies) conducted by or for the sponsor and deemed essential to FDA s approval of the NDA. This regulatory exclusivity precludes, among other things, approval of another 505(b)(2) NDA for a product with the same conditions of approval. Although obtaining such exclusivity for our product candidates could provide a competitive benefit for us, the availability of such exclusivity to competitors, if their products were to be approved before our product candidates, presents a risk. If a competing product were approved in our target indication and granted three years of exclusivity, and if the FDA were to find that our product candidate does not differ with respect to the relevant conditions of approval of the approved competing product, then approval of the 505(b)(2) NDA for our product candidate in the target indication may be delayed for as long as the competitor has exclusivity.

With a Section 505(b)(2) NDA, we also must certify to the FDA concerning any patents listed for the RLD in the Orange Book. A certification that our product candidate does not infringe the RLD s Orange Book-listed patents, or that such patents are invalid (known as a paragraph iv certification) would require providing notice of that certification to the patent holder and the sponsor of the RLD NDA, and we could then be challenged in court by the patent owner or the holder of the approved NDA for the RLD. If such a lawsuit were to be filed within a specified timeframe, it would lead to a 30-month period during which FDA would be precluded from approving our NDA.

With the approval of GOCOVRI, we will continue to be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements.

With the approval of GOCOVRI, the manufacturing, marketing, and further development of the approved product are subject to continual review by the FDA and/or analogous non-U.S. regulatory authorities. Any regulatory approval that we or our collaboration partners receive for our product candidates will be subject to limitations on the indicated uses for which the product may be marketed, and may be subject to requirements for potentially costly post-marketing follow-up studies to monitor the safety and efficacy of the product. In addition, if the FDA and/or analogous non-U.S. regulatory authorities approve any of our product candidates, we will be subject to extensive and ongoing regulatory requirements with regard to the labeling, packaging, adverse event reporting, storage, distribution, advertising, promotion, tracking, recordkeeping, and periodic reporting for our products. Further, we and our contract manufacturers of our drug products are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance and maintenance of records and documentation. Regulatory authorities must approve manufacturing facilities before they can be used to manufacture our drug products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. Certain changes to the manufacturing processes for our product candidates, if approved, would also be subject to pre-approval by regulatory authorities. In addition, if we or a third party discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, its manufacturer, or us, including but not limited to requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with regulatory requirements of the FDA and/or applicable non-U.S. regulatory authorities, we could be subject to administrative or other sanctions, including:

- warning letters or untitled letters;
- civil or criminal penalties and fines;
- injunctions;
- suspension, variation, or withdrawal of regulatory approval;
- suspension of ongoing clinical studies;
- voluntary or mandatory product recalls;
- requirements for dissemination of corrective information or modifications to promotional materials;

- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications filed by us;

- refusal to permit import or export of our products;

- restrictions on operations, including costly new manufacturing requirements; or

- seizure or detention of our products.

Regulatory requirements and policies may change, and we may need to comply with additional laws and regulations that are enacted. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we are not able to maintain regulatory compliance, we may not be permitted to market, or continue to market, our future products and our business may suffer.

Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payer cost-containment initiatives and current societal pressures regarding pharmaceutical product pricing, may negatively impact our ability to generate revenues from or could limit or prevent our product candidates commercial success.

In the United States, there have been and we expect there will continue to be a number of legislative and regulatory changes to the healthcare system that could affect our future revenue and profitability and the future revenue and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, in March 2010, the PPACA was passed, which has substantially changed how healthcare is financed by both governmental and private insurers, and has significantly impacted the U.S. pharmaceutical industry. Details of changes under the PPACA are discussed in the business heading Other healthcare regulations in Part I, Item 1, of our 2016 Annual Report on Form 10-K filed with the SEC.

Some of the provisions of the PPACA have yet to be fully implemented, and there have been legal and political challenges to certain aspects of the PPACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the individual mandate . Congress may consider other legislation to repeal or replace elements of the PPACA.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will be fully implemented in 2019. At this time it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

In addition, there have also been proposals to impose federal rebates on Medicare Part D drugs, requiring federally-mandated rebates on all drugs dispensed to Medicare Part D enrollees or on only those drugs dispensed to certain groups of lower income beneficiaries. If any of these proposals are adopted, they could result in our owing additional rebates, which could have a negative impact on revenues from sales of our products.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, have been designed to encourage importation from other countries and bulk purchasing.

We expect that the PPACA, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our existing products.

The continuing efforts of the government, insurance companies, managed care organizations, other payers of healthcare services, and patient and political groups to contain or reduce costs of healthcare may, among other things, adversely affect:

- our ability to set a price we believe is fair for our products;
- the reputation of our company;
- our ability to generate revenue and achieve or maintain profitability; and
- the availability of capital.

Our ability to commercialize our products successfully, and to attract commercialization partners for our products, will depend in significant part on the availability of adequate financial coverage and reimbursement from third-party payers, including, in the United States, governmental payers such as the Medicare and Medicaid programs, managed care organizations and private health insurers. Details of these considerations are discussed in the business heading Other healthcare regulations in Part I, Item 1, of our 2016 Annual Report on Form 10-K filed with the SEC.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs that we may join if we successfully commercialize any of our product candidates, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We intend to participate in and then will have certain price reporting obligations to the Medicaid Drug Rebate program and other governmental pricing programs.

Under the Medicaid Drug Rebate program, a manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions.

The PPACA made significant changes to the Medicaid Drug Rebate program, as discussed under the heading Other healthcare regulations in Part I, Item 1, of our 2016 Annual Report on Form 10-K filed with the SEC. On February 1, 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate program under the PPACA. These regulations became effective on April 1, 2016. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program may increase our costs and the complexity of compliance and could have a material adverse effect on our results of operations if we participate in the Medicaid Drug Rebate Program if and when we successfully commercialize any of our product candidates.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service s 340B drug pricing program in order for federal funds to be available for the manufacturer s drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge no more than the 340B ceiling price for the manufacturer s covered outpatient drugs to a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The PPACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts orphan drugs from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program. Changes to the definition of average manufacturer price and the Medicaid rebate amount under the Healthcare Reform Act and CMS s final regulations implementing those changes also could affect the 340B ceiling price calculations for any of our product candidates that we successfully commercialize and could negatively impact our results of operations.

The PPACA obligates the Secretary of the HHS to update the agreement that manufacturers must sign to participate in the 340B program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. The Health Resources and Services Administration, or HRSA, recently initiated the process of updating the agreement with participating manufacturers. The PPACA also obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program. In 2015, HRSA issued proposed omnibus guidance that addresses many aspects of the 340B program, and in August 2016, HRSA issued a proposed regulation regarding an administrative dispute resolution process for the 340B program. It is unclear when or whether the guidance or regulation will be released in final form under the Trump Administration. On January 5, 2017, HRSA issued a final regulation regarding the calculation of 340B ceiling price and the imposition of civil

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monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. The March 6, 2017 effective date of this regulation is subject to a temporary delay directed by the Trump Administration, and the regulation could be subject to further delay or other modification by the Trump Administration. Implementation of this final rule and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate, if and when we successfully commercialize any of our product candidates and if we participate in the 340B program. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by the reporting manufacturer, governmental or regulatory agencies and the courts. In the case of Medicaid pricing data, if we join the Medicaid Drug Rebate Program and become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we will be obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we would be required to offer any of our product candidates that we successfully commercialize under the 340B drug discount program.

We will be liable for errors associated with any submission of pricing data. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted any false price information to the government, we may be liable for civil monetary penalties in the amount of $178,156 per item of false information. Our failure to submit the required price data on a timely basis could result in a civil monetary penalty of $17,816 per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we will participate in the Medicaid program if we join the program if and when we successfully commercialize any of our product candidates. In the event that CMS terminates our rebate agreement, federal payments may not be available under Medicaid or Medicare Part B for any of our product candidates that we successfully commercialize.

CMS and the OIG have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that our submissions, if we participate in the federal programs if and when we successfully commercialize any of our product candidates, will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have any of our product candidates that we successfully commercialize paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs, or VA, Department of Defense, Public Health Service, and Coast Guard, referred to collectively as the Big Four agencies, and certain federal grantees, we are required to participate in the VA Federal Supply Schedule, or FSS, pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, we are obligated to make any of our product candidates that we successfully commercialize that meet the statutory definition of covered drug (biologics and single and innovator multiple source drugs) available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price, or FCP, which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the non-federal average manufacturer price, or Non-FAMP, which we will be required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of $178,156 for each item of false information. The FSS contract also contains extensive disclosure and certification requirements.

Under Section 703 of the National Defense Authorization Act for FY 2008, we will be required to pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations, and growth prospects if we successfully commercialize any of our product candidates.

If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations, and financial condition could be adversely affected.

Healthcare providers, physicians, distributors, and third-party payers play a primary role in the distribution, recommendation, and prescription of any pharmaceutical product for which we obtain marketing approval. Our arrangements with third-party payers and customers expose us to broadly applicable federal and state fraud and abuse and other laws and regulations that may constrain the business or financial arrangements through which we market, sell and distribute GOCOVRI and other products for which we may obtain marketing approval. The laws and regulations that may affect our ability to operate include:

- the federal healthcare program Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, lease, arrangement or recommendation of, any good, facility, item, or service for which payment may be made, in whole or in part, under federal healthcare programs, such as the Medicare and Medicaid programs. Liability under the Anti-Kickback Statute may be established without a person or entity having actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act;

- the federal civil and criminal false claims laws, and civil monetary penalties laws, including the federal civil False Claims Act, which prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment of government funds, or knowingly using false records or statements, to obtain payment from the federal government. In recent years, several pharmaceutical and other health care companies have faced enforcement actions under the False Claims Act for, among other things, allegedly submitting false or misleading pricing information to government healthcare programs, providing free product to customers with the expectation that the customers would bill federal programs, product and patient assistance programs, including reimbursement services, and marketing products for off-label or unapproved uses;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose obligations on HIPAA covered entities and their business associates, including mandatory contractual terms and required implementation of administrative, physical and technical safeguards to maintain the privacy and security of individually identifiable health information.

- the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program, which requires manufacturers of drugs, devices, biologicals, and medical supplies for which payment is available under Medicare, Medicaid, or the Children s Health Insurance Program (with certain exceptions) to report annually to the federal government information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members; and

- analogous state laws and regulations, such as anti-kickback, and false claims laws, which may be broader in scope and apply to items or services reimbursed by any third-party payer, including commercial insurers. Several states also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-relating activities, including the provision of gifts, meals, or other items to certain health care providers. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil, criminal and/or administrative penalties, damages, fines, disgorgement, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these or other laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, and fraud laws may prove costly.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. Moreover, the requirements governing drug pricing and reimbursement vary widely from country to country. For example, in the European Union the sole legal instrument at the European Union level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC (the Price Transparency Directive). The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in European Union member states are transparent and objective, do not hinder the free movement and trade of medicinal products in the European Union, and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not, however, provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual European Union member states. The national authorities of the individual European Union member states are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices and/or reimbursement of medicinal products for human use. Some individual European Union member states adopt policies according to which a specific price or level of reimbursement is approved for the medicinal product. Other European Union member states adopt a system of reference pricing, basing the price or reimbursement level in their territory either, on the pricing and reimbursement levels in other countries, or on the pricing and reimbursement

levels of medicinal products intended for the same therapeutic indication. Furthermore, some European Union member states impose direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some European Union member states. These countries include the United Kingdom, France, Germany, and Sweden. The HTA process in the European Union member states is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of the use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the national healthcare system. Those elements of medicinal products are compared with other treatment options available on the market.

The outcome of HTA may influence the pricing and reimbursement status for specific medicinal products within individual European Union member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of a specific medicinal product vary between the European Union member states.

In 2011, Directive 2011/24/EU was adopted at European Union level. This Directive concerns the application of patients rights in cross-border healthcare. The Directive is intended to establish rules for facilitating access to safe and high-quality cross-border healthcare in the European Union. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This could lead to harmonization between European Union member states of the criteria taken into account in the conduct of HTA in pricing and reimbursement decisions and negatively impact price in at least some European Union member states.

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

We are subject to 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 (e.g., Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure, and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions and create liability for us, including civil and/or criminal penalties, private litigation and/or adverse publicity that could negatively affect our operating results and business. In addition, we may obtain health information from third parties (e.g., healthcare providers who prescribe our products) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Although we are not directly subject to HIPAA other than potentially with respect to providing certain employee benefits we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. HIPAA generally requires that healthcare providers and other covered entities obtain written authorizations from patients prior to disclosing protected health information of the patient (unless an exception to the authorization requirement applies). If authorization is required and the patient fails to execute an authorization or the authorization fails to contain all required provisions, then we may not be allowed access to and use of the patient s information and our research efforts could be delayed. Furthermore, use of protected health information that is provided to us pursuant to a valid patient authorization is subject to the limits set forth in the authorization (e.g., for use in research and in submissions to regulatory authorities for product approvals). In addition, HIPAA does not replace federal, state, international or other laws that may grant individuals even greater privacy protections.

EU member states and other jurisdictions where we operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the EU Data Protection Directive imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. Switzerland has adopted similar restrictions. Data protection authorities from the different EU member states may interpret the applicable laws differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU. Although there are legal mechanisms to allow for the transfer of personal data from the EU to the U.S., the decision of the European Court of Justice in the *Schrems* case (Case C-362/14 Maximillian Schrems v. Data Protection Commissioner) invalidated the Safe Harbor framework and increased uncertainty around compliance with European Union restrictions on cross-border data transfers. As a result of the decision, it was no longer possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the EU to entities in the U.S. On February 29, 2016, however, the European Commission announced an agreement with the United States Department of Commerce (DOC) to replace the invalidated Safe Harbor framework with a new EU-U.S. Privacy Shield. On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and Federal Trade Commission, and making commitments on the part of public authorities regarding access to information. U.S. companies have been able to certify to the U.S. DOC their compliance with the privacy principles of the Privacy Shield since August 1, 2016. On September 16, 2016, the Irish privacy advocacy group Digital Rights Ireland brought an action for annulment of the European Commission decision on the adequacy of the Privacy Shield before the European Court of Justice (Case T-670/16). Case T-670/16 is still pending. If, however, the European Court of Justice invalidates the Privacy Shield, it will no longer be possible to rely on the Privacy Shield certification to support transfer of personal data from the European Union to entities in the US. Adherence to the Privacy Shield is not, however, mandatory. U.S.-based companies are permitted to rely either on their adherence to the EU-US Privacy Shield or on the other authorized means and procedures to transfer personal data provided by the EU Data Protection Directive.

In December 2015, a proposal for an EU General Data Protection Regulation, intended to replace the current EU Data Protection Directive, introducing new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules, was agreed between the European Parliament, the Council of the European Union, and the European Commission. The EU General Data Protection Regulation entered into force on May 24, 2016 and will apply from May 25, 2018. The EU Data Protection Regulation will increase our responsibility and liability in relation to personal data that we process and we will also face substantial fines for breaches of the data protection rules. We may be required to put in place additional mechanisms ensuring compliance with the new EU data protection rules. Furthermore, there is a growth towards the public disclosure of clinical trial data in the European Union which adds to the complexity of processing health data from clinical trials.

If we or our vendors fail to comply with applicable data privacy laws, or if the legal mechanisms we or our vendors rely upon to allow for the transfer of personal data from the EU or Switzerland to the U.S. (or other countries not considered by the European Commission to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the European Union or Switzerland is restricted.

Risks related to intellectual property

Our ability to successfully commercialize GOCOVRI and our product candidates may be materially adversely affected if we are unable to obtain and maintain effective intellectual property rights for our products and product candidates.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to GOCOVRI and our product candidates. We have sought to protect GOCOVRI and our product candidates by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years, patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the United States Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights is highly uncertain.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, the United States moved from a first to invent to a first-to-file system. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear and/or uncertain, as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the first-to-file provisions, only became effective in March 2013. In addition, the courts have only recently started to address these provisions such that the law is still developing, and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its continued implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

From time to time, we may become involved in opposition, interference, derivation, *inter partes* review, or other proceedings challenging our patent rights or the patent rights of others, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us or Allergan, without payment to us.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity, or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the patent claims of our owned or licensed patents being narrowed, invalidated, or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

For our partnered assets, like Namzaric, we may not have the right to control the prosecution of patent application, or to maintain or enforce the patent, covering our products or product candidates that we license to third parties or that we may license from third parties. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us or from us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

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

Filing, prosecuting, and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the United States. These products may compete with our product candidates in jurisdictions where we do not have any issued patents, and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Obtaining and maintaining our patent protection depends upon compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other provisions during the patent prosecution process and following the issuance of a patent. Our failure to comply with such requirements could result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case if our patent were in force.

We may become involved in lawsuits or other proceedings to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming, and if unsuccessful could materially harm our business.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property for GOCOVRI, our partnered products, and our product candidates. To counter infringement or unauthorized use, we or our licensees may be required to file infringement claims, which can be expensive and time-consuming. For example, we, Forest, Forest Laboratories, Inc., Merz Pharma GmbH & Co. KGaA, and Merz Pharmaceuticals GmbH filed patent infringement lawsuits under Forest s patents and patents owned by us and licensed to Forest, against several manufacturers of generic pharmaceuticals that have filed ANDAs with the FDA seeking approval to manufacture and sell generic versions of Namzaric® and Namenda XR®.

We anticipate that the prosecution of the lawsuits related to our partnered products and any lawsuits related to GOCOVRI will require a significant amount of time and attention of our chief executive officer and other senior executives. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the product in question. An adverse result in any litigations or proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Such a result could limit our ability to prevent others from using or commercializing similar or identical products, limit our ability to prevent others from launching generic versions of our products and could limit the duration of patent protection for our products, all of which could have a material adverse effect on our business. Also, a successful challenge to our patents could reduce or eliminate our right to receive royalties from Forest. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we or our partners are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our partners to develop, manufacture, market, and sell our product candidates and to use our proprietary technologies without infringing, misappropriating, or otherwise violating the proprietary rights or intellectual property of third parties. We or our partners may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, re-examination, *inter partes* review, post-grant review, opposition, or similar proceedings before the USPTO and its foreign counterparts. The costs of these proceedings could be substantial, and the proceedings may result in a loss of such intellectual property rights. Some of our competitors may be able to sustain the costs of complex patent disputes and litigation more effectively than we can, because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any disputes or litigation could adversely affect our ability to raise the funds necessary to

continue our operations. Third parties may assert infringement claims against us or our partners based on existing patents or patents that may be granted in the future. Under our license agreement with Allergan we are obliged to indemnify Allergan under certain circumstances and our royalty entitlements may also be reduced. Our indemnification obligation to Allergan, while subject to customary limitations, has no monetary cap, and our right to receive royalties from Allergan may be eliminated in any calendar quarter in which certain third party generic competition exists. If we or our partners are found to infringe a third-party s intellectual property rights, we could be required to obtain a license from such third-party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be unable to protect the confidentiality of our trade secrets, thus harming our business and competitive position.

In addition to our patented technology and products, we rely upon trade secrets, including unpatented know-how, technology, and other proprietary information, to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees, our partners, and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. However, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute such agreements, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. In addition, it is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement.

While to our knowledge the confidentiality of our trade secrets has not been compromised, if the employees, consultants or partners that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could be disclosed, misappropriated, or otherwise become known or be independently discovered by our competitors. In addition, intellectual property laws in foreign countries may not protect our intellectual property to the same extent as the laws of the United States. If our trade secrets are disclosed or misappropriated, it would harm our ability to protect our rights and adversely affect our business.

Risks related to Namzaric®

Under our license agreement with Allergan, if Allergan fails to successfully commercialize Namzaric® for any reason or if the license agreement with Allergan is terminated, the potential royalties we are eligible to receive under our license agreement with Allergan may not occur or be minimal, and would have a negative impact on our revenue potential and harm our business.

In November 2012, we entered into a license agreement with Allergan pursuant to which we granted Allergan a right to develop and commercialize Namenda XR® and Namzaric® in the United States. Under that agreement, we expect to receive future royalties from Allergan on the net sales of Namzaric®, starting in 2020. If for any reason Allergan fails to successfully commercialize Namzaric®, on which we are eligible to receive double digits percentage royalties, we may not receive such future royalties or receive minimal amounts, and our business will be harmed. We are also eligible to receive royalties on net sales of Namenda XR® beginning in June 2018, but we do not expect to receive such royalties, due to

the potential entry of generic versions Namenda XR®.

Under the license agreement, we are reliant on Allergan to commercialize Namzaric® and in that capacity Allergan has the discretion to:

- determine the efforts and resources that they apply towards commercialization;

- market, manufacture, and distribute the licensed products or to otherwise not perform satisfactorily in carrying out these activities; and

- to terminate the agreement without penalty and, such termination, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products.

Under the license agreement, Allergan substantially controls the intellectual property rights subject to the agreement and the current ANDA litigation and potential settlement thereof, and has economic interests different from ours. Accordingly, Allergan may manage the litigation and settlements on terms which may have a material and negative impact on our business.

We and Allergan are currently involved in ANDA litigation to enforce our intellectual property rights against generic manufacturers, who are seeking to bring generic versions of Namenda XR® and Namzaric® to the market. Further information about this litigation can be found in our Quarterly Report on Form 10-Q for the three months ended September 30, 2017 filed with the SEC. Under the terms of that license agreement, Allergan has the right to enforce such intellectual property rights and control such litigation. Specifically, Allergan has the discretion to:

- maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; and

- not adequately pursue litigation against ANDA filers or settle such litigation on unfavorable terms, and as Allergan substantially controls the current ANDA litigation and terms of settlement and has different economic interests than ours, Allergan may grant licenses to generic manufacturers that permit them to make and sell generic versions of Namenda XR® and Namzaric®, which would negatively impact the royalties we receive under our license with Allergan.

We have a right to participate in, but not control, such litigations. If Allergan decides not to enforce the intellectual property rights licensed under the agreement or the litigation is resolved in favor of the generic manufacturers or if the FDA approves the ANDA filed by the generic

manufacturers, such manufacturers may be able to market and sell the generic form of the branded drug in competition with Namenda XR® and Namzaric®. This could harm our business. Although the appeal process is not fully concluded, based on adverse trial and appellate court rulings to date with respect to Namenda XR, we do not expect to receive royalties on net sales of Namenda XR due to the potential entry of generic versions Namenda XR. The pending ANDA litigation with respect to Namzaric is at a very early stage.

Risks related to our financial condition and need for additional capital

If we do not have adequate funds to cover all of our development and commercial activities, we may have to raise additional capital or curtail or cease operations.

We have just begun to commercialize GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications, in January 2018, and it will require substantial funds to be successful. In addition, funds are required for the continued operation of our business, as we seek to advance additional product candidates through the research and clinical development to regulatory approval and commercialization. In May 2017, we entered into a Sales Agreement with Cowen and Company, LLC under which we may offer and sell our common stock having aggregate sales proceeds of up to $50 million from time to time through Cowen and Company, LLC as our sales agent. As of September 30, 2017, we have not made any sales under this facility. As of September 30, 2017, we had approximately $130.7 million in cash, cash equivalents, and investments. In addition, we received, in December 2017, $65 million in funding under the royalty-backed loan agreement signed in May 2017. We believe that our available cash, cash equivalents, and investments will be sufficient to fund our anticipated level of operations for at least the next 12 months, but there can be no assurance that this will be the case.

We have financed our operations primarily through proceeds from our license agreement with Allergan, public and private equity offerings, and, to a lesser extent, our Royalty-Backed Loan with HealthCare Royalty Partners III, L.P., or HCRP, government grants, venture debt, and benefits from tax credits made available under a federal stimulus program supporting drug development. We have devoted substantially all of our efforts to research and development, including clinical studies, of our product candidates, including GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease. We anticipate that our cash requirements will increase substantially as we:

- enhance operational, financial, and information management systems and hire more personnel, including personnel to support development of our product candidates and, our commercial operations;

- commercialize GOCOVRI, including establishing distribution, marketing, and sales capabilities;

- manufacture GOCOVRI for commercial use;

- investigate ADS-5102 (GOCOVRI) in preclinical and clinical trials for the treatment of walking impairment in patients with MS, and potentially other indications;

- conduct preclinical and clinical trials of ADS-4101 for the treatment of epilepsy (partial onset seizures);

- seek regulatory approvals for our product candidates that successfully complete clinical studies;

- continue the research, development, and manufacture of our current product candidates; and

- seek to discover or in-license additional product candidates.

If we do not have adequate funds to support these activities, our business opportunities could be hindered.

If we need additional funds to operate our business and if we cannot raise additional capital when needed, or if additional capital is not available to us on favorable terms, our stockholders may be adversely affected or our business may be harmed.

If we need additional funds to support our business and additional funding is not available under our royalty-backed loan with HCRP, or from new funding sources on favorable terms or at all, we may need to delay or

reduce the scope of our research and clinical development programs or commercialization efforts. We do not have any committed external source of funds or other support for our development efforts other than under our royalty-backed loan with HCRP, or from new funding sources or under our license agreement with Allergan, which may be terminated by Allergan upon delivery of notice. We expect to finance future cash needs through a combination of public or private equity offerings, debt financings, royalty financings, collaborations, strategic alliances, licensing arrangements, asset sales, and other marketing and distribution arrangements. Additional financing may not be available to us when we need it or it may not be available on favorable terms. If we raise additional capital through debt financings, royalty financings, collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams, or research programs or grant licenses on terms that may not be favorable to us. If we raise additional capital through equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders rights. If we raise additional capital through debt financing, in addition to the repayment of principal and interest on negotiated terms, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of, or suspend one or more of our clinical studies or research and development programs or our commercialization efforts.

We have outstanding debt backed by two of our principal assets, GOCOVRI and royalties we may receive on Namzaric, and failure by us or our royalty subsidiary to fulfill our obligations under the applicable loan agreements may cause the repayment obligations to accelerate.

In May 2017, we, through a newly formed wholly-owned subsidiary, entered into a royalty-backed note arrangement with HCRP, pursuant to which we initially borrowed $35 million and then borrowed an additional $65 million upon FDA approval and FDA s recognition in the Orange Book of the 7-year orphan drug exclusivity that GOCOVRI earned upon approval in August 2017, for the treatment of dyskinesia in patients with Parkinson s disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications.

Interest and principal on the loan will be payable from the proceeds of royalty on U.S. net sales of GOCOVRI and up to $15 million of our annual royalties from Allergan on U.S. net sales of Namzaric® starting in May 2020. The HCRP notes mature in December 2026, if not earlier repaid.

We secured the loan with rights to GOCOVRI (ADS-5102) and rights to certain payment amounts on Namzaric and the loan documents further provide for assignment into our subsidiary holding these rights to any future intellectual property, licenses, assets and agreements with respect to the manufacture, development, supply, distribution, sale and commercialization of GOCOVRI. The loan documents contain customary events of default permitting HCRP to accelerate and require mandatory prepayment of outstanding principal and interest, including: failure to timely pay principal and interest when due and payable; failure to perform specified covenants with respect to maintenance of the collateral and prohibitions on liens with respect to the collateral; limitations on payments of dividends, additional loans, acquisition or merger transactions not in accordance with the arrangement. Upon the occurrence, an event of default under the loan documents, we could be required to prepay the entire loan and, if we are not able to do so, we may lose control over certain rights and payments to GOCOVRI and royalty payments with respect to Namzaric, either of which would seriously harm our business.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. Any future revenue will depend on the successful commercialization

and sales of GOCOVRI and our product candidates, the payment of royalties to us from Allergan under terms of our licensing agreement regarding Namenda XR® and Namzaric®, or the establishment of potential future collaboration and license agreements, if any, and the achievement of any upfront or milestone payments provided thereunder. Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including:

- the level of demand for our products, which may vary significantly as they are launched and compete for position in the marketplace;

- pricing and reimbursement policies with respect to GOCOVRI and product candidates, if approved, and the competitive response from existing and potential future therapeutic approaches that compete with our product candidates;

- the cost of manufacturing our product candidates, which may vary due to a number of factors, including the terms of our agreements with contract manufacturing organizations, or CMOs;

- the timing, cost, level of investment, and success or failure of research and development activities relating to our preclinical and clinical-stage product candidates, which may change from time to time;

- expenditures that we may incur to acquire and develop additional product candidates and technologies;

- the timing and success or failure of clinical studies for competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

- the timing and magnitude of upfront and milestone payments under any potential future collaboration and licensing agreements;

- future accounting pronouncements or changes in our accounting policies; and

- changing or volatile U.S., European, and global economic environments.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated operating results and/or earnings guidance that we may provide.

Risks related to the operation of our business

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain, and motivate qualified personnel.

We are highly dependent on our chief executive officer and the other members of our executive and scientific teams. Our executives may terminate their employment with us at any time. The loss of the services of any of these people could impede the achievement of our research, development, and commercialization objectives.

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

We expect to expand our development and sales and marketing capabilities, and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2017, we had 147 full-time equivalent employees. Over the next several years, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, informational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as orphan drugs). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain, and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our

effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

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

As of December 31, 2016, we had federal and state net operating loss carryforwards of $73.0 million and $61.8 million respectively. The federal net operating loss carryforwards will begin to expire, if not utilized, beginning in 2025, and the state net operating loss carryforwards began to expire in 2016. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an ownership change, which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. It is possible that we have experienced an ownership change limitation. 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. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

We are an emerging growth company, and we cannot be certain whether the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, which was enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of our initial public offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may suffer or be more volatile.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, floods, hurricanes, fires, extreme weather conditions, medical epidemics, and other natural or manmade disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our corporate headquarters is located in California and certain clinical sites for our product candidates, operations of our existing and future partners, and suppliers are or will be located near major earthquake faults and fire zones. The ultimate impact on us, our significant partners, suppliers, and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire, or other natural or manmade disaster.

Any future operations or business arrangements with entities outside the United States present risks that could materially adversely affect our business.

If we obtain approval to commercialize any approved products or utilize CMOs outside of the United States, a variety of risks associated with international operations could materially adversely affect our business. If any product candidates that we may develop are approved for commercialization outside the United States, we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers, and regulatory requirements;
- economic weakness, including inflation or political instability in particular foreign economies and markets;
- difficulties in assuring compliance with foreign corrupt practices laws;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;

- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;

- workforce uncertainty in countries where labor unrest is more common than in the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes or typhoons, floods, and fires.

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

Despite the implementation of security measures, our internal computer systems and those of our CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access,

natural disasters, terrorism, war, and telecommunication and electrical failures. While we are not aware of any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs or commercialization efforts. For example, the loss of clinical study data from completed or ongoing clinical studies for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. While we back-up our internal computer systems periodically and store such data off-site or in the cloud, we can offer no assurance that such off-site storage of data will allow us to continue our business without interruptions to our operations, which could result in a material disruption of our drug development programs or commercialization efforts. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Risks generally associated with a company-wide implementation of information systems, including an enterprise resource planning (ERP) system, may adversely affect our business and results of operations or the effectiveness of our internal controls over financial reporting.

In support of our anticipated growth and future commercial-stage operations, we have selected and implemented a number of company-wide information systems, and may select and implement additional systems in the future, including adding new functionality to our enterprise resource planning, or ERP, and other similar systems. Many of these systems are complex and their successful and timely implementation is not assured, requires significant capital expenditures, and can be disruptive to our business operations. We recently implemented a new ERP system in addition to a new human resource information system, or HRIS. These projects required and may continue to require investment of capital and human resources and the attention of many employees who would otherwise be focused on other aspects of our business. Any deficiencies in the design and implementation of the new ERP and HRIS system could result in potentially much higher costs than we had incurred and could adversely affect our ability to develop and launch solutions, provide services, fulfill contractual obligations, file reports with the SEC in a timely manner, operate our business, or otherwise affect our controls environment. Any of these consequences could have an adverse effect on our results of operations and financial condition.

Risks related to ownership of our common stock

Our stock price may be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has fluctuated in the past and may be volatile in the future. The stock market in general and the market for securities of pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investments in our stock.

In addition, the clinical development stage of our operations may make it difficult for investors to evaluate the success of our business to date and to assess our future viability. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing GOCOVRI for the treatment of dyskinesia in patients with Parkinson s disease;
- the availability of reimbursement by payers at acceptable levels, or at all, for GOCOVRI;

- the success of competitive products or technologies;

- results of clinical studies of our product candidates or those of our competitors;

- introductions and announcements of new products and product candidates by us, our commercialization partners, or our competitors, and the timing of these introductions or announcements;

- actions taken by regulatory agencies with respect to our or our competitors products, product candidates, clinical studies, manufacturing process, or sales and marketing terms;

- variations in our financial results or those of companies that are perceived to be comparable to us;

- our revenue performance, both in absolute terms and relative to analyst and shareholder expectations;

- the success of our efforts to acquire or in-license additional products or product candidates;

- developments concerning our collaborations, including but not limited to those with our sources of manufacturing and our commercialization partners;

- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, or capital commitments;

- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our current or future products;

- our ability or inability to raise additional capital and the terms on which we raise it;

- the recruitment or departure of key personnel;

- changes in the structure of healthcare reimbursement systems;

- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our current or future products;

- market conditions in the pharmaceutical and biotechnology sectors;

- actual or anticipated changes in revenue forecasts, earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;

- trading volume of our common stock;

- sales of our common stock by us or our stockholders;

- general economic, industry, and market conditions; and

- the other risks described in this Risk Factors section.

These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. Additionally, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially and adversely affect our business, financial condition, results of operations, and growth prospects.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

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

Our executive officers, directors and current beneficial owners of 5% or more of our common stock, in the aggregate, beneficially own a significant percentage of our outstanding common stock. These persons, acting together, will be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. The interests of this group of stockholders may not coincide with the interests of other stockholders.

We will continue to incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies, and we could fail to successfully improve our systems, procedures, and controls, which could affect our operating results.

As a public company, we will continue to incur legal, accounting and other expenses associated with reporting requirements and corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, as well as new rules implemented by the SEC and the Nasdaq Stock Market LLC. We expect that we will need to continue to improve existing, and implement new operational, financial, and information management systems, procedures, and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures, or controls may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective.

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

Our stock is currently traded on Nasdaq, but we can provide no assurance that we will be able to maintain an active trading market on Nasdaq or any other exchange in the future or that the daily trading volume will be adequate to allow orderly purchases or sales of our common stock without significantly impacting the price per share. If an active market for our common stock is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all.

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

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may cease to publish research on our company at any time in their discretion. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If our operating results fail to meet the forecast of analysts, our stock price will likely decline.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price

of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions include that:

- our board of directors is divided into three classes with staggered three-year terms, which may delay or prevent a change of our management or a change in control;

- our board of directors has the right to change the size of our board of directors and to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;

- our stockholders may not act by written consent or call special stockholders meetings; as a result, a holder, or holders, controlling a majority of our capital stock would not be able to take certain actions other than at annual stockholders meetings or special stockholders meetings called by the board of directors or the chairman of the board and chief executive officer;

- our certificate of incorporation prohibits cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;

- stockholders must provide advance notice and additional disclosures in order to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror s own slate of directors or otherwise attempting to obtain control of our company; and

- our board of directors may issue, without stockholder approval, shares of undesignated preferred stock, and the ability to issue undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be our stockholders sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders sole source of gain for the foreseeable future.

SIGNATURES

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

Date: January 22, 2018

Adamas Pharmaceuticals, Inc.

By: /s/ Jennifer Rhodes
Jennifer Rhodes
Chief Business Officer and General Counsel