ENANTA PHARMACEUTICALS INC
Form 10-K
November 29, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended September 30, 2018

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number 001-35839

ENANTA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

DELAWARE	2834	04-3205099
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

500 Arsenal Street

Watertown, Massachusetts 02472

(617) 607-0800

(Address, including zip code, and telephone number, including area code, of registrant’s principal executive offices)

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

Title of each class:	Name of each exchange on which registered:

Common Stock, $0.01 Par Value The NASDAQ Stock Market LLC (NASDAQ Global Select Market)
Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of the last business day of the registrant's most recently completed second fiscal quarter, March 31, 2018, based on the last reported sale price of the registrant's common stock of $80.91 per share was $1,280,474,378. The number of shares of the registrant's Common Stock, $0.01 par value, outstanding as of November 1, 2018 was 19,423,949 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement for its 2018 Annual Meeting of Stockholders scheduled to be held on February 28, 2019, which Definitive Proxy will be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of September 30, 2018 are incorporated by reference into Part

III of this Form 10-K.

As used in this Form 10-K, “Enanta,” “the Company,” “we,” “our,” and “us” refer to Enanta Pharmaceuticals, Inc., and “MAVYRET/MAVIRET” refers to AbbVie’s HCV regimen consisting of tablets of glecaprevir/pibrentasvir, except where the context otherwise requires or as otherwise indicated. MAVYRET™, MAVIRET™, VIEKIRA PAK™, TECHNIVIE™, VIEKIRAX™, VIEKIRA XR™ and, EXVIERA™ are trademarks of AbbVie, Inc.

NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would,” and other similar e are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about overall trends, royalty revenue trends, research and clinical development plans, liquidity and capital needs and other statements of expectations, beliefs, future plans and strategies, anticipated events or trends and similar expressions. These forward-looking statements are based on our management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management’s beliefs and assumptions. These forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and discussed elsewhere in this Annual Report on Form 10-K. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this Annual Report on Form 10-K.

ENANTA PHARMACEUTICALS, INC.

ANNUAL REPORT ON FORM 10-K

For the year ended September 30, 2018

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PART I

ITEM 1. BUSINESS
BUSINESS

Overview

We are a biotechnology company that uses our robust, chemistry-driven approach and drug discovery capabilities to create small molecule drugs primarily for the treatment of viral infections and liver diseases. We discovered glecaprevir, the second of two protease inhibitors discovered and developed through our collaboration with AbbVie for the treatment of chronic hepatitis C virus, or HCV. Glecaprevir is co-formulated as part of AbbVie's newest direct-acting antiviral (DAA) combination and marketed under the tradenames MAVYRET™ (U.S.) or MAVIRET™ (ex-U.S.) (glecaprevir/pibrentasvir). Our royalties from our AbbVie collaboration and our existing financial resources provide us funding to support our wholly-owned research and development programs, which are currently focused on the following disease targets:

- respiratory syncytial virus, or RSV, the most common cause of bronchiolitis and pneumonia in children under one year of age in the U.S., resulting in an estimated 57,000 to 125,000 U.S. hospitalizations each year;
- non-alcoholic steatohepatitis, or NASH, a liver disease estimated to affect approximately 1.5% to 6.5% of the population in the developed world (which translates to approximately 5 to 20 million individuals in the U.S. alone);
- primary biliary cholangitis, or PBC, a chronic liver disease that slowly destroys bile ducts in the liver, which affects an estimated 17,000 individuals in the U.S.; and
- hepatitis B virus, or HBV, the most prevalent chronic hepatitis, which is estimated to affect approximately 250 million individuals worldwide.

We had $325.1 million in cash, cash equivalents and marketable securities at September 30, 2018. In fiscal 2018, we earned $191.6 million in per-product royalties on AbbVie's net sales of its HCV regimens and we earned the remaining $15.0 million milestone payment from AbbVie upon reimbursement approval for MAVIRET™ in Japan. We expect our existing financial resources and future royalties from our AbbVie collaboration will allow us to continue to fund our wholly-owned research and development programs for the foreseeable future.

Our Wholly-Owned Programs

Our wholly-owned research and development programs are in virology, namely RSV and HBV, and in liver disease (non-virology), namely NASH and PBC:

- RSV: We discovered EDP-938, a potent N-protein inhibitor of activity of both major subgroups of RSV, referred to as RSV-A and RSV-B, and have tested it as our first clinical candidate for RSV. We believe EDP-938 is differentiated from fusion inhibitors currently in development for RSV because N-protein inhibitors directly target the viral replication process of RSV and have demonstrated high barriers to resistance against RSV in vitro.
  - In our fiscal 2018, we completed a Phase 1 clinical study demonstrating that EDP-938 was generally safe and well tolerated over a broad range of single and multiple doses with good pharmacokinetic data.
  - We initiated a Phase 2a challenge study of EDP-938 in October 2018. The challenge study will test the effect of EDP-938 on healthy volunteers who will be infected with RSV and then treated with EDP-938 or placebo during the course of the study. Primary and secondary outcome measures include changes in viral load measurements and change of baseline symptoms.
  - Preclinical data demonstrated that EDP-938 is a potent inhibitor of both RSV-A and RSV-B activity, maintaining antiviral activity post-infection while presenting a high barrier to resistance in vitro.

- NASH and PBC: We are working on multiple compounds that selectively bind to and activate the farnesoid X receptor, or FXR. We plan to develop these compounds, referred to as FXR agonists, for use in the treatment of NASH and PBC, both of which are liver diseases with very few therapeutic options. Our lead FXR agonist, EDP-305, represents a new class of FXR agonists designed to take advantage of increased binding interactions with the receptor. We believe this class is significantly different from other FXR agonists in clinical development.
  - In October 2017, we announced results of a Phase 1a/b clinical study of EDP-305, which was generally safe and well tolerated over a broad range of single and multiple doses with pharmacokinetic data supporting once daily oral dosing. Additional data from this study were also presented at the 2018 NASH-TAG conference and the International Liver Congress™ (ILC) 2018. The study included 98 healthy volunteer subjects, or HV subjects, and 48 subjects who were obese and with or without pre-diabetes or type 2 diabetes, whom we refer to as subjects with presumptive non-alcoholic fatty liver disease, or PN subjects.
  - We have presented data at the 2017 and 2018 annual meetings of the American Association for the Study of Liver Diseases (AASLD), the 2017 and 2018 NASH-TAG conferences and the 2017 and 2018 ILC conferences that demonstrated that EDP-305 is a highly selective FXR agonist and shows more potent activity in a variety of in vitro and in vivo NASH models compared to the most advanced NASH candidate in development today, obeticholic acid, or OCA.
  - We initiated a Phase 2 clinical study, known as ARGON-1, of EDP-305 in NASH patients and a Phase 2 clinical study, known as INTREPID, of EDP-305 in PBC patients.
    - EDP-305 has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for the treatment of NASH patients with liver fibrosis and separately for the treatment of PBC.
  - In addition, we are pursuing research in other classes of FXR agonists as well as other mechanisms that may provide therapeutic benefit in NASH, any of which could be used in combination therapies for NASH.
- HBV: We also have a program to discover and develop new chemical entities for the treatment of HBV. Our initial focus is on core inhibitors, a mechanism with early clinical validation. In November 2018, we announced our first clinical candidate for HBV. EDP-514 is an HBV core inhibitor, also known as a core protein allosteric modulator or capsid assembly modulator.
  - EDP-514 was selected from our lead class of HBV compounds that are characterized by potent antiviral activity. In vitro, they are capable of preventing the establishment of cccDNA, are pan-genotypic, are active against known nucleos(t)ide resistant mutants, and are additive to synergistic with nucleoside analogs and other core inhibitors. Members of this class have also demonstrated excellent reduction in HBV titers in a chimeric mouse model with human liver cells.
  - In addition, we are also seeking patent protection and conducting preclinical experiments with compounds we have discovered that use other mechanisms to target HBV. We believe that it may be necessary to utilize more than one compound/mechanism for the treatment of HBV and therefore we are pursuing multiple approaches.

We have utilized our internal chemistry and drug discovery capabilities to generate all of our development-stage programs.

Our Out-Licensed Products

Through our Collaborative Development and License Agreement with AbbVie, we have developed and out-licensed to AbbVie two protease inhibitor compounds that have been clinically tested, manufactured, and commercialized by AbbVie. To date, we have earned all $330.0 million milestone payments under the agreement related to clinical development and commercialization regulatory approvals of these regimens in major markets.

- Glecaprevir: Glecaprevir is the protease inhibitor we discovered that was developed by AbbVie in a fixed-dose combination with its NS5A inhibitor, pibrentasvir, for the treatment of HCV. This combination, currently marketed under the brand name MAVYRET™ (U.S.) and MAVIRET™ (ex-U.S.) and referred to in this report as MAVYRET/MAVIRET, is a novel, once daily, all oral, fixed-dose, ribavirin-free treatment for HCV genotypes 1-6, or GT1-6, which is referred to as being pan-genotypic. In the U.S., EU and Japan it was approved as an 8-week treatment for patients without cirrhosis and new to treatment. Today, these patients are estimated to represent the majority of HCV patients in developed country markets.

Since August 2017, substantially all of our royalty revenue has been derived from AbbVie's net sales of MAVYRET/MAVIRET. Our ongoing royalty revenues from this regimen consist of annually tiered, double-digit, per-product royalties (see Note 7 in Notes to Consolidated Financial Statements) on 50% of the calendar year net sales of the 2-DAA glecaprevir/pibrentasvir combination in MAVYRET/MAVIRET. These royalties are calculated separately from the royalties on AbbVie's paritaprevir-containing regimens.

- Paritaprevir: Paritaprevir is the protease inhibitor contained in AbbVie's initial HCV treatment regimens sold under the tradenames VIEKIRAX® (ex-U.S.) and VIEKIRA PAK® (U.S.) (paritaprevir/ritonavir/ ombitasvir/dasabuvir). These regimens are no longer being actively marketed in markets where MAVYRET/MAVIRET is approved and reimbursed. AbbVie's paritaprevir-containing regimens were first approved and sold in the U.S. in December 2014. Through our 2017 fiscal year end, our royalty revenues were generated substantially through worldwide net sales of these regimens.

Our Strategy

Our primary objective is to become a leader in the field of viral infections and liver diseases in order to provide new treatments for patients with unmet medical needs. Our focus is on antiviral targets for viruses such as RSV and HBV as well as liver diseases, such as NASH and PBC. All of these disease areas involve significant market opportunities and have attracted the research and development efforts of many competitors. Our strategy includes the following key elements:

- Develop novel treatment options for RSV, NASH, PBC and HBV. We have potential candidates in clinical development for RSV, NASH and PBC. We completed a Phase 1 clinical study of our lead RSV candidate, EDP-938, and have initiated a Phase 2a challenge study in RSV in October 2018. We also completed a Phase 1 a/b clinical study of EDP-305, our lead FXR agonist, and initiated two Phase 2 clinical studies of this compound during fiscal 2018 – one in NASH patients and one in PBC patients. In addition, we recently selected a development candidate for HBV, EDP-514, which we plan to test in a Phase 1 a/b clinical study initiating in 2019.
- Invest in research and development of additional product candidates in RSV, NASH/PBC and HBV. We are continuing to invest significant resources in our RSV, NASH, PBC and HBV research programs in an effort to identify and advance additional novel compounds that have the potential to address significant unmet medical needs in these disease areas. We may clinically explore other diseases where our assets could play a role. In addition, we may seek to augment our product candidate pipeline through the acquisition or in-licensing of external assets and/or technologies in one or more of our disease areas of focus.
- Use our existing resources and future cash flow from our AbbVie collaboration to fund our research and development activities. Our existing financial resources and future royalty payments from our AbbVie collaboration will provide us substantial resources to fund our research and development programs for the foreseeable future.

These resources will allow us to continue to advance compounds in clinical development as well as to progress the most promising candidates at least through proof-of-

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concept for further development as a monotherapy or in combinations with other therapeutic agents when we believe such combinations will provide the most promising opportunities.

- Collaborate, where and when appropriate, with pharmaceutical partners to create combination therapies and accelerate the development and commercialization of our proprietary compounds. We are prepared to join forces, where and when appropriate, with collaborators with compounds targeting other mechanisms of action in diseases such as NASH and HBV, where there is the potential for better treatments with combination therapies. Our decisions regarding our proprietary programs will be based on the results of our early phase clinical studies and the potential for combinations with one or more drugs targeting other mechanisms of action in these diseases.

Our Research and Development Pipeline

The following table summarizes our product development pipeline in our virology and liver disease programs:

Our RSV Program

Background and Overview of RSV

Respiratory syncytial virus, or RSV, is a virus that infects the lungs and represents a serious unmet medical need in infants and children, as well as immune-compromised individuals and the elderly. RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lung) and pneumonia in children under 1 year of age in the United States. Each year, 57,000 to 125,000 patients in the U.S. are hospitalized due to RSV infection. In one large U.S.-based study, RSV infection in children was associated with 20% of hospitalizations, 18% of emergency

department visits, and 15% of pediatric office visits for acute respiratory infections in the November-April timeframe. Though a prophylactic monoclonal antibody-based treatment is available for infants considered at high risk for RSV infection, this study found that most young children affected by RSV infection were previously healthy, and thus would not normally be considered for prophylaxis. There are currently no safe and effective therapies for already established RSV infection. Several companies are seeking new antiviral treatments for RSV infection in adult and pediatric settings and others are developing vaccines.

Scientific Background

RSV is a single-stranded, negative-sense RNA virus. The RSV genome consists of ten genes that encode for 11 proteins, namely NS1, NS2, N, P, M, SH, G, F, M2-1, M2-2, and L. The F and G proteins are the predominant target proteins for RSV vaccines. Similarly, small molecule therapeutics have focused primarily on the F (or fusion) protein, while some efforts have targeted the N and L proteins. There are two major subgroups of RSV, designated RSV-A and RSV-B, each of which contains numerous genotypes. Both groups are viewed as capable of causing RSV infections that can result in hospitalization.

EDP-938 and Our Approach to the Treatment of RSV

While a number of companies are developing potential approaches geared towards the F protein (or fusion protein, responsible for mediating viral entry of RSV into host cells), we are focused on other mechanisms, such as the N-protein pathway, that target the replication process of RSV. It is possible that N-protein inhibitors may also be effective treatments at later stages of infection. We are currently the only company with an N inhibitor in clinical development.

Through our internal chemistry efforts, we identified a clinical candidate, EDP-938. During preclinical studies, EDP-938 demonstrated a greater than 4-log reduction in viral load in an animal model challenged with RSV. Further, EDP-938 maintained antiviral potency across all clinical isolates tested in vitro, as well as virus that was resistant to fusion inhibitors. The compound inhibited RSV at a post-entry replication step and maintained its activity in vitro when given 24 hours post infection. In addition, combination studies of EDP-938 with other types of RSV inhibitors, such as fusion inhibitors, showed synergistic antiviral effects.

During fiscal 2018, we initiated and completed a Phase 1 clinical study of EDP-938. On November 1, 2018, we presented full Phase 1 data at the 11th International Respiratory Syncytial Virus Symposium. The Phase 1, randomized, double-blind, placebo (PBO)-controlled, first-in-human study was conducted to evaluate the safety, tolerability, and pharmacokinetics (PK) of single- and multiple- (7 days) ascending doses (SAD: 50 - 800 mg and MAD: 100 - 600 mg once daily and 300 mg twice daily) and food effect (FE) of EDP-938 in healthy subjects. In the SAD phase, 50 subjects [EDP-938 (n=38) and PBO (n=12)] were enrolled in 6 dose cohorts; in the MAD phase, 40 subjects [EDP-938 (n=30) and PBO (n=10)] were enrolled in 5 dose cohorts. Overall, no safety concerns were reported in 68 healthy subjects receiving a broad range of single and multiple doses of EDP-938. Headache was the most frequently reported AE during the SAD and MAD phases. There were no SAEs, and AEs were of mild intensity, with none leading to study drug discontinuation. EDP-938 was rapidly absorbed and exposure increased with increasing single and multiple dosing, resulting in a PK profile suitable for once or twice daily oral dosing regardless of food. In the MAD phase, half-life ranged from 12.9 to 17.6 hours, and at doses comparable to those under study in the Phase 2a trial, and mean trough levels were approximately 30x higher than the EC90 of EDP-938 against RSV-infected human cells.

Based on the results above, we initiated a Phase 2a challenge study of EDP-938 in October 2018. In this randomized, double-blind, placebo-controlled, human challenge study, up to 114 healthy adult subjects will be randomized into 1 of 3 arms (1:1:1) and will be dosed for 5 days. All subjects will be infected with RSV-A Memphis 37b virus, and approximately 76 subjects will receive EDP-938 and 38 subjects will receive placebo. Arm 1 will receive placebo, Arm 2 will receive a single 500 mg loading dose of EDP-938 followed by 300 mg doses twice daily, and Arm 3 will receive a 600 mg dose daily.

Our FXR Program in NASH and PBC

Background and Overview of NASH and PBC

Non-alcoholic fatty liver disease, or NAFLD, is the accumulation of excessive fat in liver cells in the form of triglycerides, a process known as hepatic steatosis, that is not associated with alcohol abuse. It is normal for the liver to contain some fat. However, if more than 5%-10% of the liver's weight is fat, then it is called a fatty liver. A subgroup of NAFLD patients have liver cell injury and inflammation (steatohepatitis) in addition to excessive fat. Progression of this condition leads to non-alcoholic steatohepatitis, or NASH. Patients with NASH can develop fibrosis, a fibrous scarring of the liver, and ultimately cirrhosis of the liver. Typically scored on a scale of 1-4, also referred to as F1-F4, fibrosis in its earlier stages has been shown to be reversible, but in its most advanced stage results in cirrhosis, which is understood to be a more advanced, irreversible scarring of the liver, potentially leading to hepatocellular carcinoma (HCC) or requiring a liver transplant. NASH is widely considered to be the liver expression of metabolic diseases related to type 2 diabetes, insulin resistance, obesity, hyperlipidemia and hypertension.

Stages of Liver Injury

According to the World Gastroenterology Organization Global Guidelines 2014, NASH is an increasingly common chronic liver disease with worldwide distribution that is closely associated with diabetes and obesity, which have both reached epidemic proportions. It is estimated that there are at least 1.46 billion obese adults worldwide. Approximately 3%-5% of individuals in the U.S. are estimated to have progressed to NASH, 20% of whom are likely to develop cirrhosis. NASH and NAFLD are now considered the number one cause of liver disease in Western countries.

Currently, there are no approved treatments for NASH. While patients presenting with NASH are counseled on lifestyle modifications, new effective treatments are urgently needed, particularly in the setting of advanced fibrosis and cirrhosis. We expect significant competition from other companies in the development of treatments for NASH and related conditions. Currently, Intercept Pharmaceuticals, Genfit, Gilead and Allergan (Tobira) have compounds in one or more Phase 3 trials in NASH. In addition, many Phase 2 and earlier stage studies of other classes of compounds are underway by various companies.