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): September 27, 2018

SPERO THERAPEUTICS, INC.
(Exact Name of registrant as specified in its charter)

Delaware	**001-38266**	**46-4590683**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

675 Massachusetts Avenue, 14th Floor
Cambridge, Massachusetts 02139
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (857) 242-1600

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

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

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

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

☐ 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 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

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. ☒

Item 7.01 Regulation FD Disclosure.

On September 27, 2018, Spero Therapeutics, Inc. (the "Company") issued a press release announcing final data from its Phase 1 dose-selection clinical trial of SPR994. A copy of the press release is attached hereto as Exhibit 99.1. Additional information about these final results is set forth in Exhibit 99.2.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit 99.1 Press Release, dated September 27, 2018.

Exhibit 99.2 Additional information regarding final data from the Company's Phase 1 dose-selection clinical trial of SPR994.

Forward Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the initiation, timing, progress and results of the Company's preclinical studies and clinical trials and the Company's research and development programs, including statements regarding management's assessment of the results of such preclinical studies and clinical trials, the timing of initiating a Phase 3 clinical trial of SPR994, the potential of SPR994, the Company's cash forecast and anticipated expenses and the sufficiency of the Company's cash resources. In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intent," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether the Company's product candidates will advance through the preclinical development and clinical trial process on a timely basis, or at all; whether the results of such trials will warrant submission for approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether the Company's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; and other factors discussed in the "Risk Factors" set forth in filings that we periodically make with the U.S. Securities Exchange Commission. The forward-looking statements included in this press release represent the Company's views as of the date of this press release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

SIGNATURE

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

SPERO THERAPEUTICS, INC.

Date: September 27, 2018

By: /s/ Joel Sendek
Joel Sendek
Chief Financial Officer and Treasurer

Spero Announces Positive SPR994 Phase 1 SAD/MAD Final Results

- *Multiple ascending dose clinical data supports advancement of 600 mg TID dose for pivotal Phase 3 clinical trial, planned for initiation around year-end 2018*
- *600 mg dose provides greater drug exposure than 300 mg dose with comparable safety profile*

CAMBRIDGE, Mass., September 27, 2018 (GLOBE NEWSWIRE) — Spero Therapeutics, Inc. (Nasdaq:SPRO) (Spero), a multi-asset clinical-stage biopharmaceutical company focused on developing and commercializing novel antibiotics to treat multi-drug resistant bacterial infections, today reported positive results from a final analysis of its Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) clinical trial of SPR994, its investigational oral carbapenem product candidate designed for the treatment of Gram-negative infections. The study was conducted in healthy volunteers to assess the safety, tolerability and pharmacokinetics of SPR994. Dose escalation within the MAD portion of the Phase 1 clinical trial demonstrated that 600 mg of SPR994 provides greater drug exposure than was observed in the first dosing cohort of 300 mg while maintaining a favorable safety profile. The final data expand on the interim data announced in July 2018, and the Company anticipates the data will support the advancement of SPR994 at a dose of 600 mg administered three times per day (TID) into a pivotal Phase 3 clinical trial, which the Company expects to initiate around year-end 2018 in patients with complicated urinary tract infections (cUTI).

“The final Phase 1 data demonstrate compelling pharmacokinetics, safety and tolerability for SPR994 at all doses tested,” said Ankit Mahadevia, M.D., CEO of Spero Therapeutics. “There is a significant unmet need for new oral therapies to treat drug resistant infections. We believe SPR994 has the potential to be an important clinical and economic addition in treating these patients by helping to transition patients out of the hospital or reducing the need for hospitalization altogether. We look forward to our scheduled pre-Phase 3 meeting with the FDA, after which we plan to advance SPR994 into a pivotal Phase 3 clinical trial around year-end 2018 in patients with cUTI, subject to feedback from the FDA.”

The Phase 1 SAD/MAD clinical trial assessed the safety, tolerability and pharmacokinetics of orally administered SPR994. The Phase 1 clinical trial enrolled 124 healthy adult volunteers into 14 SAD cohorts with SPR994 given orally as single doses ranging from 100 mg to 900 mg daily and 2 MAD cohorts with SPR994 given orally at doses of 300 mg and 600 mg every 8 hours for 14 days. Final results demonstrated a linear and proportional increase in plasma exposure over the dose range tested, with no accumulation over 14 days of repeated dosing. Furthermore, the administration of SPR994 in the fed or fasting state did not substantially alter the plasma drug exposure, indicating that SPR994 can likely be administered without regard to meals. Consistent with the predominantly renal elimination of SPR994, peak urine concentrations were approximately 50 to 100-fold higher than maximum concentrations in plasma, supporting SPR994’s potential utility as treatment for patients with cUTI.

The final Phase 1 results build upon the interim results announced in July 2018. Those results demonstrated that in the SAD portion of the Phase 1 clinical trial, SPR994 was well tolerated at doses ranging from 100 mg to 900 mg daily. Those results also showed that in the MAD portion of the trial, the 300 mg TID dose of SPR994 demonstrated mean free drug plasma concentrations of tebipenem, SPR994’s active metabolite, that remained above the MIC90 for the relevant bacterial pathogens for >50% of an 8-hour dosing interval, which supports the selected TID dosing interval.

No serious adverse events were reported in the Phase 1 clinical trial. Oral administration of SPR994 was well tolerated at all doses tested within the trial, and the Phase 1 results are consistent with available clinical and post-marketing data for Orapenem® and other approved intravenous (IV) carbapenem antibiotics. Orapenem® is currently approved in Japan for the treatment of pediatric infections and has the same orally bioavailable active ingredient as SPR994, tebipenem pivoxil.

Spero has scheduled a pre-Phase 3 meeting with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2018. Following discussions with the FDA, Spero plans to initiate a pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018. Spero believes that the approval of an oral carbapenem with activity against resistant bacterial pathogens, including those exhibiting resistance to fluoroquinolones and cephalosporins, would support a shift in care of cUTI patients from the inpatient to the outpatient setting.

About SPR994

SPR994 is Spero's novel investigational oral formulation of tebipenem, a carbapenem-class antibiotic marketed by Meiji Seika Pharma Co. Ltd. (Meiji) in Japan as Orapenem® since 2009 for pediatric infections limited to pneumonia, otitis media and sinusitis. Carbapenems are an important class of antibiotics because they have been demonstrated to be safe and effective against drug-resistant Gram-negative bacterial infections. Spero has completed a Phase 1 clinical trial of SPR994, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study to enable dose selection for Spero's planned pivotal Phase 3 clinical trial. Pending discussions from a pre-Phase 3 meeting with the FDA in the fourth quarter of 2018, Spero plans to initiate a pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018 in support of a new drug application (NDA). In preclinical studies, SPR994 has shown potent antibiotic activity against Gram-negative bacteria, including *E. coli*-producing extended-spectrum beta-lactamases (ESBLs) and ESBL-producing *Klebsiella pneumoniae*, similar to IV-administered ertapenem. Approximately 1,200 subjects have been dosed with tebipenem in clinical and pharmacologic studies conducted by Meiji during its development of tebipenem in Japan. In addition, available post-marketing outcomes data report of tebipenem in 3,540 pediatric patients with pneumonia, otitis media or sinusitis, and these data are consistent with the safety profile of tebipenem as observed in the clinical trial conducted by Meiji.

About Spero

Spero Therapeutics is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multidrug-resistant (MDR) bacterial infections.

Spero is advancing SPR994, a carbapenem-class antibiotic, which is designed to be the first broad-spectrum oral antibiotic for use in adults to treat MDR Gram-negative infections.

Spero is also advancing its Potentiator Platform, which it believes will enable the development of drugs that will expand the spectrum and potency of existing antibiotics, including formerly inactive antibiotics, against Gram-negative bacteria. The product candidates are two IV-administered agents, SPR741 and SPR206, designed to treat MDR Gram-negative infections in the hospital setting.

Spero is also advancing SPR720, its novel oral therapy product candidate designed for the treatment of pulmonary non-tuberculous mycobacterial (NTM) infection, an orphan infectious disease indication.

For more information, visit ***https://sperotherapeutics.com***.

Forward Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the initiation, timing, progress and results of the Company's preclinical studies and clinical trials and the Company's research and development programs, including statements regarding management's assessment of the results of such preclinical studies and clinical trials, the timing of initiating a Phase 3 clinical trial of SPR994, the potential of SPR994, the Company's cash forecast and anticipated expenses and the sufficiency of the Company's cash resources. In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intent," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether the Company's product candidates will advance through the preclinical development and clinical trial process on a timely basis, or at all; whether the results of such trials will warrant submission for approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether the Company's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; and other factors discussed in the "Risk Factors" set forth in filings that we periodically make with the U.S. Securities Exchange Commission. The forward-looking statements included in this press release represent the Company's views as of the date of this press release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

Spero Investor Contact:

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Director, Investor Relations
857-242-1547
IR@sperotherapeutics.com

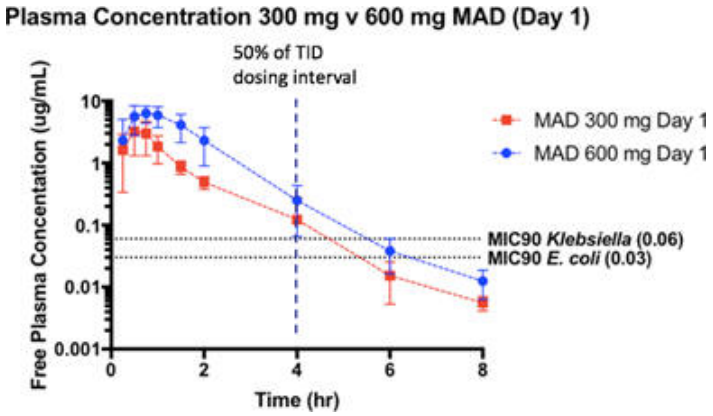
Additional information regarding final data from the Company's Phase 1 dose-selection clinical trial of SPR994

Our completed Phase 1 clinical trial of SPR994 assessed the safety, tolerability and pharmacokinetics of orally administered SPR994, including the impact of utilizing immediate and sustained release formulations to optimize the pharmacokinetic profile of the drug. In addition, the trial evaluated the impact of administration of SPR994 in the fed and fasted state. We believe the final data from the trial, which expand on the interim data we announced in July 2018, are sufficient to enable us to refine a pharmacokinetic/pharmacodynamic (PK/PD) model to support the selection of an SPR994 dosing regimen for our planned pivotal Phase 3 clinical trial of SPR994 based on plasma drug concentrations and accounting for inter-patient PK variability. Specifically, we believe the final data from the trial support the advancement of SPR994 at a dose of 600 mg administered three times per day (TID) into a pivotal Phase 3 clinical trial. We have scheduled a pre-Phase 3 meeting with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2018 and, subject to FDA feedback, we expect to submit an investigational new drug application with the FDA and initiate a pivotal Phase 3 clinical trial of SPR994 for the treatment of complicated urinary tract infections (cUTI) around year-end 2018.

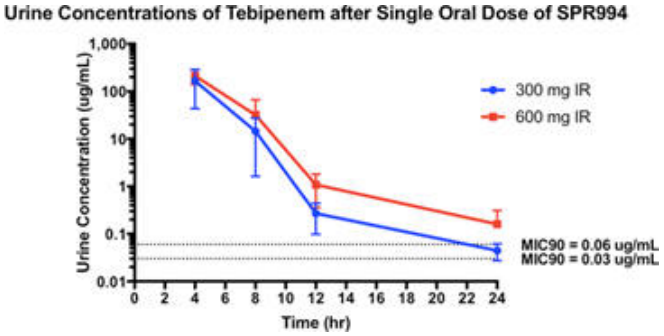
The Phase 1 clinical trial enrolled 124 healthy adult volunteers into 14 single-ascending dose (SAD) cohorts and two multiple-ascending dose (MAD) cohorts evaluating formulations of SPR994 at single oral doses ranging from 100 mg to 900 mg in the SAD cohorts and repeated doses of 300 mg and 600 mg orally TID for 14 days in the MAD cohorts. Final results from the Phase 1 clinical trial demonstrated that:

- Oral administration of SPR994 was well-tolerated at all doses tested. A linear and proportional increase in plasma concentration was observed following oral administration of doses ranging from 100 mg to 900 mg of SPR994, with no accumulation over 14 days of repeated dosing.
- Administration of SPR994 following a high fat meal did not substantially alter the plasma exposure as compared with administration to volunteers in a fasted state. We believe these data indicate that SPR994 can likely be administered without regard to meals.
- The mean plasma free drug concentrations versus time observed following administration of SPR994 300 mg and 600 mg of the immediate-release dose formulation to healthy adult volunteers are presented in the figure below. The mean plasma concentrations of tebipenem remained above the MIC_{90} for the relevant bacterial pathogens for >50% of an 8-hour dosing interval (TID administration). We believe this exposure level would be effective as a treatment for cUTI based on preclinical PD models.

Tebipenem Pharmacokinetic Profile Following Administration of 300 mg and 600 mg of SPR994 (IR) to Healthy Volunteers (Mean +/- SD)



- Renal elimination of tebipenem at 300 mg and 600 mg TID resulted in urine concentrations that were approximately 50 to 100-fold higher than the maximum plasma free drug concentrations following the administration of 300 mg and 600 mg of SPR994 and in excess of the MIC_{90} of the most prevalent urinary pathogens for greater than the 8-hour dosing interval, as presented in the figure below. We believe this provides an added margin of exposure for the treatment of cUTI with SPR994 600 mg administered orally TID.



- The tebipenem plasma free drug exposure predicted following the administration of SPR994 600 mg orally TID (expressed as a function of the dosing interval, fAUC/tau) was comparable to that observed following the administration of ertapenem (1 g) administered intravenously every 24 hours in a third-party clinical trial that did not involve a comparison of ertapenem with SPR994. Because both ertapenem and tebipenem exhibit time and concentration-dependent antibacterial activity, we believe that the similar plasma free drug exposures over time mitigate the risk of comparing the efficacy of oral tebipenem with IV-administered ertapenem in our planned pivotal Phase 3 clinical trial of SPR994.
- The most common adverse event observed in the Phase 1 trial was diarrhea/soft stool, occurring in 13/87 (14.9%) of SPR994-treated subjects. These events were of mild severity (generally a single episode of loose stool), largely occurred early (day 1-2) during repeated dose treatment, and were resolved within 24 hours despite continued treatment in the MAD portion of the trial. There was no notable difference in the frequency, severity, or duration of diarrhea in subjects receiving 300 mg or 600 mg of SPR994 TID and there were no discontinuations. The observed frequency of diarrhea/soft stool is generally in line with prior experience with amoxicillin-clavulanate (9%), Orapenem® (9.5%) and other carbapenem antibiotics, including ertapenem (9.2-10.3%), in third-party clinical trials. There were no reported cases of *clostridium difficile* infections.
- 3/87 (3.4%) of SPR994-treated subjects experienced a treatment emergent adverse event (TEAE) of elevated alanine transaminase (ALT) levels at or above the upper limit of normal (ULN). All cases of TEAEs of ALT elevations occurred in the MAD portion of the trial with two subjects experiencing elevations <3x ULN and a single subject in the 300 mg cohort reaching a maximum value of >3x, which is the ULN. Of note, the ALT level in this subject declined despite continued dosing with SPR994 300 mg TID through day 14. There were no Hy's law cases or other evidence of drug-induced liver injury. ALT elevation is a known class effect of carbapenem antibiotics, including Orapenem (reported as <1% in clinical trials and the post-marketing surveillance study), and the data received to date for SPR994 suggest that its effect on ALT levels is comparable to that observed with other carbapenems. In third-party clinical trials that did not involve a comparison of such drugs with SPR994, ALT elevations were reported for ertapenem (8%), ceftaroline (2%) and aztreonam (10-38%) (as reported in the LiverTox database maintained by the National Institute of Diabetes and Digestive and Kidney Diseases), as well as for doripenem (4.0%) and ceftazidime-avibactam (4.6%) (as reported in the FDA summary basis for approval of ceftazidime-avibactam (Avycaz®)).