Assembly Biosciences Announces Promising Interim Results from Two Clinical Trials Evaluating Highly Potent Next-Generation Core Inhibitor Candidates ABI-H3733 and ABI-4334

December 19, 2022

- *In initial ABI-H3733 cohort of 50 mg in 28-day Phase 1b study, six of eight HBV patients on treatment reached lower limit of quantification for HBV DNA by day 21 and patients showed a mean reduction of 3.1 logs in plasma HBV DNA*
- *Initial ABI-4334 Phase 1a single-dose 30 mg cohort demonstrated pharmacokinetic profile supportive of once-daily oral dosing and provides early indication that ABI-4334's very high potency seen preclinically can be accessed clinically*
- *No serious adverse events or significant laboratory abnormalities including alanine aminotransferase (ALT) elevation were observed in either study*
- *Given potent antiviral activity in the initial 50 mg cohort, second 25 mg cohort ongoing in Phase 1b trial of ABI-H3733 to explore dose-response curve; 100 mg cohorts ongoing for both studies with further data expected in Q1 2023*

SOUTH SAN FRANCISCO, Calif., Dec. 19, 2022 (GLOBE NEWSWIRE) -- Assembly Biosciences, Inc. (Nasdaq: ASMB), a clinical-stage biotechnology company developing innovative, investigational therapeutics targeting hepatitis B virus (HBV) and other viral diseases, today announced promising interim efficacy, safety and pharmacokinetic (PK) results from two ongoing clinical studies of its investigational next-generation HBV core inhibitors, a Phase 1b clinical study of ABI-H3733 (3733) and a Phase 1a clinical study of ABI-4334 (4334).

“We are excited to see that these interim results from ongoing Phase 1 studies of our next-generation core inhibitors 3733 and 4334 are exceeding our expectations for key elements of the clinical profile we’re looking for to impact chronic HBV infection,” said John McHutchison, AO, MD, chief executive officer of Assembly Bio.

Assembly Bio specifically designed 3733 and 4334 to optimize potency against both new virus production (first mechanism) and formation of covalently closed circular DNA (cccDNA), the viral reservoir (second mechanism). Both compounds have demonstrated significantly increased potency preclinically against both mechanisms compared to first-generation core inhibitors. This increased potency, particularly against cccDNA formation, is critical to Assembly Bio’s HBV strategy to bring finite therapies and cures for those living with chronic HBV (cHBV) infection.

“In this first look at antiviral activity for 3733 in the Phase 1b study, we are seeing steep declines in HBV DNA at the low starting dose of 50 mg,” continued Dr. McHutchison. “The antiviral activity from this cohort against the first mechanism surpasses both what we demonstrated preclinically for 3733 as well as what we saw clinically in similar time frames with our first-generation core inhibitors at much higher doses. We are also highly encouraged by the initial pharmacokinetic data from our first-in-human clinical study of our most potent core inhibitor, 4334, which show the potential to reach high levels of activity against both mechanisms clinically at a low dose.”

Jason Okazaki, president and chief operating officer and CEO-elect of Assembly Bio, concluded, “With 100 mg cohorts of both 3733 (28-day dosing) and 4334 (single dose) underway, we are eager to see and share data in early 2023 that we anticipate will drive the optimal dose selection to maximize activity against both mechanisms of action. While early, we believe the interim results in both studies are an encouraging indication that the preclinical potency documented for our next-generation core inhibitors against the second mechanism of cccDNA formation will translate into the clinic with longer-term dosing.”

Complete results of these clinical trials, when available, together with ongoing nonclinical and chronic toxicity studies, will inform future clinical development planning for Assembly Bio’s next-generation core inhibitor programs.

Phase 1b Study for 3733 – Study ABI-H3733-102

The ongoing Phase 1b clinical trial is a randomized, multi-center, double-blind and placebo-controlled study evaluating the safety, PK and antiviral activity of 3733, including changes in HBV DNA and other viral parameters associated with 3733 treatment in adults with cHBV infection who are treatment naïve or off treatment. Patients were randomized 8:2 between the new tablet formulation of 3733 and placebo for a period of 28 days. The patient population for the data included here consists primarily of e-antigen negative patients. The study remains externally blinded, so individual patient data are not provided.

The dose selected for the first cohort was 50 mg. Given the potent antiviral activity observed at 50 mg, a 25 mg dose was

selected for the second cohort to further explore the dose response curve of 3733. A dose of 100 mg has been selected for the third cohort, for which dosing is ongoing with initial data anticipated in the first quarter of 2023.

50 mg Cohort Efficacy (Viral Nucleic Acids):

As of the data cutoff date of December 18, 2022, dosing in the 3733 Phase 1b trial has been completed for all 10 patients in the first cohort of 50 mg. Nine of 10 patients enrolled were HBeAg negative, so efficacy data are provided for these patients. Interim efficacy results from this cohort at the data cutoff date include HBV DNA, HBV RNA and antigen measurements for all patients for the full 28-day dosing period.

In the 50 mg cohort, six of eight patients receiving 3733 achieved HBV DNA less than the lower limit of quantification (<LLOQ) within 21 days, with a mean decline in HBV DNA over the treatment period of approximately 3.1 logs. Data on HBV RNA declines were limited due to low baseline levels in predominantly e-antigen negative patients.

25 mg Cohort Efficacy (Viral Nucleic Acids):

The second cohort, evaluating a dose of 25 mg, is fully enrolled. Nine of 10 patients enrolled were HBeAg negative, so efficacy data are provided for these patients. In the five patients that have so far completed 28 days of treatment, the mean reduction in HBV DNA was approximately 1.9 logs. Data on HBV RNA levels were not available as of the data cutoff date.

50 and 25 mg Cohorts (Safety, PK and Viral Antigens):

Safety data reported here reflect data received for both cohorts through the data cutoff date. In these initial cohorts, all treatment-emergent adverse events (AEs) and laboratory abnormalities reported were Grade 1 or Grade 2. Further, no AEs led to treatment discontinuation, and no clinically significant ECG abnormalities or patterns of AEs or lab abnormalities were noted.

The observed PK for the new tablet formulation of 3733 was consistent with predictions from preclinical studies, providing exposure equivalent to the liquid formulation evaluated in the Phase 1a study for 3733. Clinical PK exposures exhibited dose-proportional increases from 25 mg to 50 mg, as measured by maximum concentration (C_{max}) and area-under-curve (AUC).

As expected given the 28-day dosing period, limited changes in viral antigens were observed in both the 50 mg and 25 mg cohorts.

Phase 1a Study for 4334 – Study ABI-4334-101

The Phase 1a clinical trial is a randomized, blinded and placebo-controlled study evaluating the safety, tolerability and PK of 4334 following single ascending dose and multiple ascending dose administration in healthy subjects. The objectives of the study include assessment of the proportion of subjects with AEs, premature treatment discontinuation due to AEs and abnormal laboratory results.

Dosing has completed for all eight subjects in the initial 30 mg single dose cohort. In this cohort, 4334 had a mean half-life of 24 hours, supporting once-a-day (QD) dosing. Based on the PK data from this initial cohort and preclinical studies, daily minimum plasma trough concentrations (C_{min}) are projected to achieve double-digit multiples of the protein-adjusted EC_{50} for both antiviral activity and against cccDNA formation at a low dose of 4334.

In this initial cohort, treatment-emergent AEs and laboratory abnormalities were mild to moderate and all were considered not related to study treatment. There were no clinically significant ECG abnormalities or patterns of AEs or laboratory abnormalities noted.

A dose of 100 mg has been selected for the second single-dose cohort. Dosing for the second cohort is complete and initial data from this cohort are anticipated in the first quarter of 2023.

About Assembly Biosciences

Assembly Bio is a clinical-stage biotechnology company pioneering the development of novel therapeutics for serious viral diseases. Assembly Bio is advancing a leading portfolio of more potent, next-generation core inhibitor drug candidates that aim to break the complex viral replication cycle of hepatitis B virus (HBV) to achieve finite and potentially curative therapies for the 296 million people living with HBV worldwide. The company's research pipeline includes differentiated antiviral approaches against HBV/hepatitis delta virus and herpesviruses. For more information, visit assemblybio.com.

Forward-Looking Statements

The information in this press release contains forward-looking statements that are subject to certain risks and uncertainties that could cause actual results to materially differ. These risks and uncertainties include: Assembly Bio's ability to successfully execute its previously announced reprioritization and restructuring activities, including the CEO transition; potential adverse legal,

reputational, operational and financial effects on Assembly Bio resulting from the reprioritization and restructuring activities; Assembly Bio's ability to initiate and complete clinical studies involving its therapeutic product candidates, including studies contemplated by Assembly Bio's collaboration agreements, in the currently anticipated timeframes; safety and efficacy data from clinical studies may not warrant further development of Assembly Bio's product candidates; clinical and nonclinical data presented at conferences may not differentiate Assembly Bio's product candidates from other companies' candidates; results of nonclinical studies may not be representative of disease behavior in a clinical setting and may not be predictive of the outcomes of clinical studies; continued development and commercialization of ABI-H3733, if successful, in the China territory will be dependent on, and subject to, Assembly Bio's collaboration agreement governing this activity in the China territory; Assembly Bio's ability to maintain financial resources necessary to continue its clinical studies and fund business operations; any impact that the COVID-19 pandemic may have on Assembly Bio's business and operations, including initiation, enrollment and continuation of its clinical studies or timing of discussions with regulatory authorities; and other risks identified from time to time in Assembly Bio's reports filed with the U.S. Securities and Exchange Commission (the SEC). You are urged to consider statements that include the words may, will, would, could, should, might, believes, hopes, estimates, projects, potential, expects, plans, anticipates, intends, continues, forecast, designed, goal or the negative of those words or other comparable words to be uncertain and forward-looking. Assembly Bio intends such forward-looking statements to be covered by the safe harbor provisions contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. More information about Assembly Bio's risks and uncertainties are more fully detailed under the heading "Risk Factors" in Assembly Bio's filings with the SEC, including its most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. Except as required by law, Assembly Bio assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Contacts

Investor and Corporate:
Shannon Ryan
SVP, Investor Relations, Corporate Affairs and Alliance Management
(415) 738-2992
sryan@assemblybio.com

Media:
Sam Brown Inc.
Hannah Hurdle
(805) 338-4752
ASMBMedia@sambrown.com