Research by Assembly Biosciences and Academic Collaborators Published in Hepatology Indicates cccDNA Turnover Time May Enable Hepatitis B Cures Following Finite Therapy

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Data demonstrate turnover is faster than previously described for cccDNA, a necessary component required for the establishment and persistence of HBV infection

SOUTH SAN FRANCISCO, April 06, 2020 (GLOBE NEWSWIRE) -- Assembly Biosciences, Inc. (NASDAQ: ASMB), a clinical-stage biotechnology company developing innovative therapeutics targeting hepatitis B virus (HBV) and diseases associated with the microbiome, today announced that results from a research study evaluating the turnover rate of covalently closed circular DNA (cccDNA), which plays a pivotal role in the establishment and persistence of HBV infection, has been published in *Hepatology*, the journal of the American Association for the Study of Liver Diseases (AASLD). The study was led by Qi Huang, PhD, the Company's Vice President of Virology Discovery, and was conducted in collaboration with Professors Jinlin Hou, Jian Sun, and Bin Zhou of Nanfang Hospital, Southern Medical University in Guangzhou, China. The article is entitled *Rapid Turnover of HBV cccDNA Indicated by Monitoring Emergence and Reversion of Signature-Mutation in Treated Chronic Hepatitis B Patients* and is available online with open access.

"This important translational research study provides us with valuable insight as we and others work to advance potential curative therapeutic regimens for patients with HBV infection," said Richard Colonno, PhD, Executive Vice President and Chief Scientific Officer of Virology Operations at Assembly. "It shows that cccDNA turnover occurs in months, not years as once thought, supporting the possibility of finite therapy if cccDNA replenishment can be effectively blocked. Combining core inhibitors, which inhibit cccDNA establishment, with nucleos(t)ide therapy may provide a regimen that is able to more fully suppress viral replication and inhibit the establishment of new cccDNA. We plan to evaluate this hypothesis as we begin transitioning patients off treatment later this year in our ongoing Phase 2 long-term extension study (211) with our lead HBV therapeutic, ABI-H0731, and as we work to advance the clinical development of our second and third core inhibitor candidates."

Understanding the turnover time of the intranuclear preexisting cccDNA pool is important in evaluating and assessing potential curative treatment regimens for chronic HBV infection. This study used a molecular genetic approach to monitor the appearance and disappearance of resistance mutations as a biomarker of cccDNA turnover in longitudinal liver biopsies and serum samples obtained from patients from two clinical trials. HBV virion DNA, cccDNA, and HBV pgRNA were isolated and sequenced from clinical samples. The genetic makeup of cccDNA pools were shown to turnover in as little as three to four months, consistent with frequent cccDNA replacement in chronically-infected patients and suggesting that regimens which fully inhibit cccDNA replenishment may achieve a finite cure through decay of the existing cccDNA pool during treatment. Further, a strong correlation was observed between cccDNA composition and serum pgRNA in paired liver and serum samples, suggesting that serum HBV pgRNA is a primary surrogate marker of cccDNA when liver biopsies are unavailable.

About Assembly Biosciences' HBV Core Inhibitor Portfolio
Assembly's HBV portfolio includes several clinical-stage small molecules, all of which are inhibitors of the HBV core protein targeting multiple steps of the life cycle of HBV. ABI-H0731, a first-generation core inhibitor, is advancing in Phase 2 clinical development. In Phase 2 clinical trials, ABI-H0731 administered with nucleos(t)ide therapy has been well-tolerated and has shown statistically superior antiviral activity in HBV DNA suppression compared to nucleos(t)ide therapy alone and also significant declines in pgRNA that may indicate decreases in cccDNA levels. Assembly's HBV portfolio also includes two clinical-stage second-generation candidates ABI-H2158 and ABI-3733.

About Assembly Biosciences
Assembly Biosciences, Inc. is a clinical-stage biotechnology company developing innovative therapeutics targeting hepatitis B virus (HBV) and diseases associated with the microbiome. The HBV program is focused on advancing a new class of potent, oral core inhibitors that have the potential to increase cure rates for chronically infected patients. The microbiome program is developing novel oral live microbial biotherapeutic candidates with Assembly's fully integrated platform, including a robust process for strain identification and selection, GMP manufacturing expertise and targeted delivery to the lower gastrointestinal tract with the GEMICEL® technology. For more information, visit assemblybio.com.

Forward-Looking Statements
The information in this press release contains forward-looking statements regarding future events, including statements about the therapeutic potential of our HBV core inhibitor product candidates, predictions on the turnover time of preexisting cccDNA pools, and the timing of the initiation of and the availability of data from our ongoing and planned clinical trials. Certain forward-looking statements may be identified by reference to a future period or by use of forward-looking terminology such as "intend," "may," "potential," "promise," and "strategy."
Assembly 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. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. These risks and uncertainties include, among others: the components, timing, cost and results of clinical trials and other development activities involving our product candidates; the impact of the coronavirus pandemic on planned and on-going clinical trials, and results of earlier preclinical and nonclinical studies may not be predictive of future clinical studies results. More information about the risks and uncertainties faced by Assembly are more fully detailed under the heading "Risk Factors" in Assembly's Annual Report on Form 10-K for the year ended December 31, 2019 filed with the Securities and Exchange Commission. Except as required by law, Assembly assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Contacts
Assembly Biosciences, Inc.
Amy Figueroa, CFA
Investor Relations Consultant
(415) 366-5158

afigueroa@assemblybio.com

Solebury Trout
Luke Brown
(646) 378-2944
lbrown@troutgroup.com

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