Data for Assembly Biosciences' First and Second Generation HBV Core Inhibitors in Development for the Treatment of Chronic Hepatitis B Highlighted in Late-Breaker Poster Session at AASLD 2019

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- *ABI-H0731 + nucleos(t)ide analogs (Nrtl) in patients with chronic Hepatitis B demonstrated favorable longer-term tolerability, greater reductions in HBV DNA and HBV pregenomic (pg) RNA in Phase 2 studies than Nrtl alone*
- *Significant declines in HBV pgRNA, a surrogate marker of cccDNA, were associated with reductions in hepatitis B viral antigens*
- *Company to host conference call today at 8:30am ET*

SOUTH SAN FRANCISCO, Calif., Nov. 11, 2019 (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, announced that data for its first and second generation HBV core inhibitors were highlighted during today's late-breaker poster session at the American Association for the Study of Liver Diseases (AASLD) Annual Meeting (The Liver Meeting®) in Boston, Massachusetts. The posters featured final 24-week results and interim long-term data from the Phase 2 studies of ABI-H0731 (731). Additionally, the company presented initial data from the first dose cohort in the ongoing Phase 1b study of ABI-H2158 (2158). The posters will be made available on the Investors page of the assemblybio.com website.

"It's encouraging to see innovation and evolution coming to this field, given the impact of HBV infection globally and limited ability of current therapies to fully suppress the virus," said Dr. Kosh Agarwal, Kings College Hospital, London. "Assembly presented the first data to suggest that a core inhibitor can potentially reduce cccDNA levels, as reflected by observed reductions in pgRNA and HBV viral antigens. As physicians treating these patients, we would all like to see new regimens that could bring about viral suppression rapidly and completely without sacrificing safety and tolerability. Moving forward, we hope to reach a point where viral reservoirs are depleted, and a cure can be achieved. I look forward to seeing future results from the ongoing studies of Assembly's core inhibitor candidates."

"We are pleased to present these data at AASLD demonstrating that the longer-term administration of 731+Nrtl was well tolerated and has shown greater reductions in HBV DNA and pgRNA than the current standard of care," said John McHutchison, AO, MD, Chief Executive Officer and President of Assembly. "I am particularly excited to now see the evidence suggesting a core inhibitor could potentially produce an effect on the Hepatitis B virus that is considerably different from what is seen with Nrtl therapy alone-- such as the clear and significant declines in pgRNA. Even more important is that these significant pgRNA declines were strongly associated with reductions in other viral antigens, suggesting cccDNA pools are diminishing. As treatment in the open-label extension study continues, we hope to observe continued viral DNA and pgRNA suppression that we believe may be associated with further declines in viral antigens. Over the course of 2020, treatment will be withdrawn to see if viral suppression can be sustained in some patients."

ABI-H0731
This poster included final 24 week data from HBeAg-positive patients in studies *ABI-H0731-201* (Study 201 Nrtl-suppressed patients) and *ABI-H0731-202* (Study 202 Nrtl-naïve patients) in addition to interim data from an ongoing open-label extension study *ABI-H0731-211* (Study 211), where all patients receive combination 731+Nrtl therapy.

Of the 97 patients completing Study 201 or Study 202, 87 are currently receiving 731+Nrtl and have been treated for at least 16 weeks in Study 211 (cumulative duration of treatment with 731+Nrtl of 16 to >40 weeks). 731 was well-tolerated when administered in combination with Nrtl therapy. Overall, 26 out of 58 patients reported no adverse events (AEs). The remaining patients reported AEs that were Grade 1 or 2 and no serious AEs have been reported to date.

Study 201 and Study 202
As previously reported in the literature, the vast majority of long-term Nrtl treated patients continue to harbor low level infectious virus and this was confirmed in Study 201 patients at the time of enrollment. Final Week 24 results from the HBeAg-positive patients (n=47) demonstrated that, among those with detectable DNA at baseline, 22/27 (81%) of 731+Nrtl treated patients achieved target not detected (TND) by Week 24 vs 0/12 (0%) Nrtl only treated patients ($p<0.001$), as measured with a highly sensitive PCR assay (lower limit of quantification (LLOQ) 5 = IU/mL). These results indicate that the addition of 731 reduced viral burden to levels not achieved by Nrtl therapy alone.

Final Week 24 results from HBeAg-positive patients in Study 202 (n=25) demonstrated faster and deeper HBV DNA declines in patients receiving 731+entecavir (ETV) than those receiving ETV alone. Statistically significant reductions of pgRNA were observed by Week 2 with 731+ETV ($p<0.001$).

Study 211
Longer-term treatment with 731+NrtI resulted in deeper reductions in HBV DNA and pgRNA. The 21 of 25 patients from Study 202 now in Study 211 demonstrated mean HBV DNA and pgRNA declines from baseline of 6.3 logs and 3.0 logs, respectively, at Week 48.

A significant finding based on interim data from Study 211 is the observed correlation between the degree of pgRNA reductions and viral antigen declines. Eleven of 21 (52%) patients from Study 202 now on Study 211 who have been treated with 731+Nrtl for 16-60 weeks have achieved decreases in pgRNA of >3 logs. The results in the tables below demonstrate that these larger declines in pgRNA were strongly associated with observed reductions in viral antigens. Because cccDNA is the only known source of pgRNA, the deeper decline of pgRNA levels may therefore indicate a reduction in cccDNA pools.

Number	<40 U/L	Log_{10} Decrease	Mean Log Reductions at Last Time Point (range)	Patients Exhibiting ≥0.5 Log Decline (%)

Patients	ALT	pgRNA	HBeAg	HBcrAg	HBsAg	HBeAg	HBcrAg	HBsAg
11	10	>3.0	1.03 (0.0-2.5)	1.42 (0.0-3.1)	0.86 (0.0-3.6)	9 (82)	10 (91)	6 (55)
8	8	2.0-3.0	0.34 (0.1-0.7)	0.45 (0.1-1.0)	0.14 (0.0-0.5)	2 (25)	6 (75)	1 (13)
2	2	<2.0	0.15 (0.9-1.8)	0.29 (0.3-0.3)	0.17 (0.0-0.3)	0 (0)	0 (0)	0 (0)

Of the 27 Nrtl-suppressed HBeAg-positive patients receiving 731+Nrtl for at least 40 weeks in Study 201 and who are now in Study 211, 18 (67%) have achieved HBV DNA TND + pgRNA <35 U/mL, along with significant declines in HBeAg and HBcrAg levels.

Safety Overview
731 was well-tolerated in both HBeAg-positive and -negative patients when administered with a Nrtl for 24 weeks with no serious AEs reported. Five patients receiving 731+Nrtl reported a rash (four Grade 1 and one Grade 2). No associated systemic signs or laboratory abnormalities were observed, and all patients continued treatment through Week 24. Overall, laboratory abnormalities observed were of Grade 1 or 2 severity and occurred in similar proportions of patients across the two treatment groups. With longer-term ongoing treatment in Study 211, interim data indicated that the nature, frequency and severity of AEs and laboratory abnormalities observed were similar to the initial 24 week treatment period.

ABI-H2158
The Phase 1b study of 2158 is currently enrolling HBeAg positive patients in sequential dose cohorts of nine patients, with each cohort randomized to receive oral 2158 or placebo (7:2) once daily for 14 days. The poster details interim safety data and antiviral activity from the initial cohort receiving the lowest dose of 2158 at 100 mg. These interim data demonstrated potent antiviral activity at this initial dose level, reflected by mean declines from baseline to day 15 of 2.3 $\log_{10}$ [range 1.7 – 3.0] and 2.1 $\log_{10}$ [range 1.5 - 2.7] in HBV DNA and pgRNA respectively.

No serious AEs, dose limiting toxicities or premature discontinuations have been reported to date. All treatment emergent adverse events (TEAEs) were Grade 1. One patient assigned to placebo and three patients on 2158 reported TEAEs that resolved without intervention: dizziness, fatigue, rash, headache and upper abdominal pain. Observed steady-state exposures were in excess of the $EC_{90's}$ for *in vitro* antiviral and cccDNA assays. We believe that the safety and pharmacokinetic (PK) data and parameters from this interim analysis support once daily administration and the continued evaluation of 2158 across the planned dose cohorts in patients with chronic HBV infection. The Phase 1b study is expected to be completed in the first quarter of 2020.

Conference Call and Webcast Information
Assembly will host a conference call and live audio webcast today at 8:30 am ET. The live audio webcast and the presentation can be accessed through the Events & Presentations page in the Investors section of the company's website at assemblybio.com. Alternatively, participants can dial (866) 438-0453 (domestic) or +1 (409) 220-9366 (international) and refer to conference ID 4283686.

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-compliant banking and production, 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 clinical and therapeutic potential of our HBV core inhibitor product candidates, 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 "expected," "may" and "potential." 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: Assembly's expectations regarding sustained benefits and antiviral reductions of patients in its clinical trials; the scientific theory for our therapeutics is unproven and novel; outcomes of clinical studies are uncertain; results observed in earlier preclinical and nonclinical studies and early clinical studies, including with respect to tolerability results, may not be predictive of future clinical studies results; the components, timing, cost and results of clinical trials and other development activities involving our product candidates; the duration and results of regulatory review of those candidates by the FDA and foreign regulatory authorities; whether our cash resources will be sufficient to fund continuing operations for the periods and/or trials; and the possible impairment of, or inability to obtain, intellectual property rights and the costs of obtaining such rights from third parties. More information about the risks and uncertainties faced by Assembly are more fully detailed under the heading "Risk Factors" in Assembly's Quarterly Report on Form 10-Q for the quarter ended September 30, 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.

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