Assembly Biosciences Provides Update on its Core Inhibitor Pipeline, Reports Fourth Quarter and Year End 2022 Financial Results and Recent Highlights

March 22, 2023

- *Prioritization of core inhibitor candidate ABI-4334 and pausing of core inhibitor candidate ABI-H3733 based on data to date from ongoing clinical Phase 1 studies of both candidates and chronic toxicology observation for ABI-H3733*
- *Phase 1a complete clinical data for all ABI-4334 dose cohorts expected in April 2023*
- *Advancing expanded research portfolio, with additional development candidate nomination anticipated in 2023 and IND/CTA submission for herpesvirus candidate ABI-5366 planned for the first half of 2024*

SOUTH SAN FRANCISCO, Calif., March 22, 2023 (GLOBE NEWSWIRE) -- Assembly Biosciences, Inc. (Nasdaq: ASMB), a clinical-stage biotechnology company developing innovative antiviral therapeutics targeting serious viral diseases, today provided an update on its investigational next-generation hepatitis B virus (HBV) core inhibitors, ABI-H3733 (3733) and ABI-4334 (4334), and reported financial results and recent highlights for the fourth quarter and year ended December 31, 2022.

“Last year, we accelerated our research pipeline and advanced our clinical pipeline of next-generation, highly potent HBV core inhibitors, 3733 and 4334,” said Jason Okazaki, chief executive officer and president of Assembly Bio. “While the clinical antiviral activity seen in HBV patients receiving 3733 in our Phase 1b trial is impressive, our objective has always been to prioritize the strongest candidate in a data-driven manner. Based on the data from our ongoing clinical and nonclinical studies, we are focusing on 4334 given its greater potency and encouraging clinical profile emerging from the initial cohorts in the Phase 1a study. We plan to evaluate and share data for the remaining multiple-dose cohort from that study in April.”

In the 100 mg cohort of 3733 in a 28-day Phase 1b study, all seven HBeAg negative chronic HBV (cHBV) patients that have completed dosing reached the lower limit of quantification for HBV DNA by day 21. In the Phase 1a study of 4334, all single-dose cohorts and the first multiple-dose cohort of 100 mg are complete. In these cohorts, 4334’s pharmacokinetic (PK) profile continues to be supportive of once-daily oral dosing and of providing exposures sufficient to potently inhibit both HBV DNA and covalently closed circular DNA (cccDNA) formation. No serious adverse events (AEs) or patterns of clinically significant AEs or laboratory abnormalities have been observed in either clinical study. However, a time-dependent toxicity in one species was observed in a nonclinical chronic toxicology study for 3733 that was not observed in the previous 28-day toxicology study.

“Beyond core inhibitors, we also achieved important research milestones in 2022, leveraging our virology expertise to broaden our discovery pipeline to include additional mechanisms of action targeting hepatitis B and hepatitis delta, as well as two programs outside of viral hepatitis targeting herpesviruses,” continued Mr. Okazaki. “We are thrilled with the progress of these programs, including the recent nomination of 5366, our first herpesvirus development candidate which we expect to move into the clinic for the potential treatment of patients who suffer from high-recurrence genital herpes during the first half of 2024. High-recurrence genital herpes is a disease for which current treatments are only partially effective and a new therapeutic hasn’t been approved in decades. We are excited at the opportunity to advance treatment options for this significant unmet medical need and expect to build upon our research progress with the nomination of a second development candidate from our expanded pipeline later this year.”

4334 and 3733 Clinical Data Updates

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 been completed for all subjects in all single-dose cohorts (30 mg, 100 mg, 200 mg and 400 mg) and both multiple-dose cohorts of 100 mg and 200 mg, with data pending for the 200 mg multiple-dose cohort.

Based on data available for the single-dose and 100 mg multiple-dose cohorts through March 21, 2023, 4334 continued to show a half-life supportive of once-a-day (QD) dosing. In addition, based on PK data from these cohorts and preclinical studies, daily minimum plasma trough concentrations (Cmin) are projected to achieve double-digit multiples over protein-adjusted EC_{50} for both antiviral activity and against cccDNA formation within the dose range studied in the Phase 1a study.

Through March 21, 2023, treatment-emergent AEs and laboratory abnormalities were mild to moderate and there were no patterns of AEs or laboratory abnormalities noted and no clinically significant ECG abnormalities reported.

A dose of 200 mg was selected for the second and final multiple-dose cohort. Dosing for this cohort is complete and data from this cohort are anticipated in April.

4334 was internally discovered and developed by Assembly Bio and designed to optimize potency against both new virus production and formation of cccDNA, the viral reservoir, and has a distinct chemical scaffold from 3733.

Phase 1b Study for 3733 (Study ABI-H3733-102 and Nonclinical Toxicology Studies)

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 of HBeAg negative patients. The study remains externally blinded, so individual patient data are not provided. Initial data for the 25 and 50 mg cohorts were reported in December 2022.

100 mg Cohort Efficacy (Viral Nucleic Acids), Safety and PK:

In the 3733 Phase 1b trial, as of March 21, 2023, enrollment was completed with 11 patients randomized to treatment. 10 of the 11 patients enrolled were HBeAg negative so efficacy data are not provided for the single HBeAg positive patient. Dosing has been completed for seven HBeAg negative patients receiving 100 mg 3733 and interim efficacy data are presented here for these seven patients. Interim efficacy results from this cohort include HBV DNA, HBV RNA and antigen measurements for the full 28-day dosing period.

In the 100 mg cohort, all seven HBeAg negative patients receiving 3733 who have completed treatment achieved HBV DNA less than the lower limit of quantification (<LLOQ) within 21 days. As all of these subjects achieved HBV DNA <LLOQ, the mean decline in HBV DNA over the treatment period of approximately 3.0 logs is reflective of both the baseline DNA levels and the lower limit of the quantifiable range in this cohort. Data on HBV RNA declines were limited due to low baseline levels in HBeAg negative patients. As expected given the 28-day dosing period, limited changes in viral antigens were observed.

Safety data for all 11 patients in the 100 mg cohort for 3733 through March 21, 2023, are reported. All treatment-emergent 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.

Available PK data indicated that exposures exhibited dose-proportional increases in the dose range from 25 mg QD to 100 mg QD.

Nonclinical Toxicology Studies for 3733:

In parallel with the Phase 1b study, a 26-week nonclinical chronic toxicology study has been ongoing and revealed a time-dependent toxicity in one species that was not observed in the previous 28-day toxicology study. Assembly Bio continues to evaluate the data, however, proceeding with longer-term dosing of 3733 in a Phase 2 study would require further assessment and likely an additional chronic toxicology study in another species, which would add cost and time to the development timeline for 3733.

Fourth Quarter 2022 and Recent Highlights

- Appointed Jason Okazaki as chief executive officer and president and a member of the board of directors, succeeding John McHutchison, AO, MD, with Dr. McHutchison continuing to serve on the board of directors
- Reported interim clinical data from two next-generation HBV core inhibitor candidates in December 2022:
    - Interim Phase 1b data of 3733 in patients with cHBV infection
    - Initial Phase 1a data of 4334 in healthy subjects
- Initiated all cohorts of 3733 in Phase 1b study in patients with cHBV infection and 4334 in Phase 1a study in healthy subjects
- Announced nomination of Assembly Bio's first herpesvirus development candidate, ABI-5366 (5366), a long-acting herpes simplex virus type 2 (HSV-2) helicase inhibitor targeting high-recurrence genital herpes, for advancement to IND-enabling studies
- Presented four posters, including two late-breaking posters, at AASLD The Liver Meeting™ in November 2022

Anticipated Milestones and Events

- Complete final 200 mg multiple-dose cohort for 4334 and report additional Phase 1a clinical data in April
- Nominate one additional development candidate from the expanded research portfolio in 2023
- Complete IND/CTA submission for 5366 in the first half of 2024

Fourth Quarter 2022 and Year End Financial Results

- **Cash, cash equivalents and marketable securities** were $91.6 million as of December 31, 2022, compared to $108.7 million as of September 30, 2022, and $174.6 million as of the year ended December 31, 2021. The company's cash position is projected to fund operations into mid-2024.
- **Research and development expenses** were $70.0 million for the year ended December 31, 2022, compared to $68.5 million in 2021. The increase year-over-year is primarily due to a one-time reduction in costs in 2021 related to the microbiome program.
- **General and administrative expenses** were $24.1 million for the year ended December 31, 2022, compared to $28.8 million in 2021. The decrease is primarily due to a reduction in professional and consulting fees and a reduction in stock-based compensation expense.
- **Net loss attributable to common stockholders** was $93.1 million, or $1.92 per basic and diluted share, for the year ended December 31, 2022, compared to $129.9 million, or $3.00 per basic and diluted share in 2021.

About Assembly Biosciences
Assembly Biosciences is a clinical-stage biotechnology company dedicated to the development of innovative small molecule antiviral therapeutics designed to change the path of serious viral diseases and improve the lives of patients worldwide. The company's hepatitis B virus (HBV) pipeline includes potent, next-generation HBV core inhibitors in clinical development, which are designed to disrupt the virus' replication cycle at several key points with the aim of achieving finite treatment and functional cures. Assembly Bio's HBV and hepatitis delta virus (HDV) pipeline also includes two complementary approaches, a viral entry inhibitor and an oral, liver-focused, interferon-alpha receptor agonist, with potential application for both HBV and as chronic suppressive therapy for HDV, which is associated with significantly increased disease burden for HBV/HDV patients. The herpesvirus pipeline addresses two serious consequences associated with herpesvirus infections, high-recurrence genital herpes and transplant-associated herpesviruses. Led by an accomplished team of leaders in virologic drug development, Assembly Bio is committed to improving outcomes for patients struggling with the serious, chronic impacts of HBV, HDV and herpesvirus infections. 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 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 or nonclinical 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; 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.

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ASSEMBLY BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands except for share amounts and par value)

	December 30, 2022	December 31, 2021
ASSETS		
Current assets		
Cash and cash equivalents	$52,418	$45,627
Marketable securities – short-term	39,192	101,000
Accounts receivable from collaborations	944	336
Prepaid expenses and other current assets	4,413	7,241
Total current assets	96,967	154,204
Marketable securities – long-term	—	27,972
Property and equipment, net	743	1,139
Operating lease right-of-use (ROU) assets	3,195	6,042
Other assets	889	1,703
Total assets	**$101,794**	**$191,060**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$2,493	$2,659
Accrued research and development expenses	3,122	3,400
Other accrued expenses	7,317	6,863
Operating lease liabilities – short-term	3,364	3,151
Total current liabilities	16,296	16,073
Deferred revenue	2,733	2,733
Operating lease liabilities – long-term	101	3,325
Total liabilities	**19,130**	**22,131**
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.001 par value; 150,000,000 and 100,000,000 shares authorized as of December 31, 2022 and December 31, 2021, respectively; 48,894,973 and 48,120,437 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	49	48
Additional paid-in capital	807,938	800,728
Accumulated other comprehensive loss	(803)	(419)
Accumulated deficit	(724,520)	(631,428)
Total stockholders' equity	82,664	168,929
Total liabilities and stockholders' equity	**$101,794**	**$191,060**

ASSEMBLY BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands except for share and per share amounts)

	Year Ended December 31,	
	2022	**2021**
Collaboration revenue	$ —	$6,254
Operating expenses		
Research and development	69,980	68,524
General and administrative	24,134	28,780
Impairment of goodwill and indefinite-lived intangible asset	—	41,638
Total operating expenses	94,114	138,942
Loss from operations	**(94,114)**	**(132,688)**
Other income		
Interest and other income, net	1,022	302
Total other income	1,022	302
Loss before income taxes	**$(93,092)**	**$(132,386)**
Income tax benefit	—	2,531
Net loss	**$(93,092)**	**$(129,855)**
Other comprehensive loss		
Unrealized loss on marketable securities	(384)	(149)
Comprehensive loss	**$(93,476)**	**$(130,004)**
Net loss per share, basic and diluted	$(1.92)	$(3.00)
Weighted average common shares outstanding, basic and diluted	48,409,265	43,280,383