Arbutus Announces Preliminary Phase 1a/1b Clinical Trial Results for AB-506, an Oral Capsid Inhibitor in Development for People with Chronic Hepatitis B

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Results demonstrate that AB-506 is a potent capsid inhibitor

Phase 1a/1b clinical trial to continue with the enrollment of further cohorts

Conference call and webcast scheduled today at 4:45 pm ET

WARMINSTER, Pa., July 15, 2019 (GLOBE NEWSWIRE) -- Arbutus Biopharma Corporation (Nasdaq: ABUS), an industry-leading Hepatitis B Virus (HBV) therapeutic solutions company, today announced preliminary results from a Phase 1a/1b clinical trial in healthy subjects and two cohorts of chronic hepatitis B (CHB) subjects who received AB-506 monotherapy. A detailed analysis of these Phase 1a/1b preliminary results will be submitted for presentation at a future scientific meeting later this year.

William H. Collier, President and Chief Executive Officer of Arbutus, stated, “Preliminary results from this first Phase 1a/1b clinical trial demonstrate that AB-506 is a potent oral capsid inhibitor. These results also support our confidence in its potential to contribute to the inhibition of HBV replication as part of a combination regimen.”

Summary of preliminary results with AB-506

- No serious adverse events (SAEs) or clinically significant safety findings were observed in healthy subjects (N=33). Importantly, ALT levels and other liver function tests remained normal throughout the 10 days of dosing in healthy subjects.

- Mean HBV DNA and HBV RNA decreases at Day 28 (end of treatment) ranged from -2.0 log (160mg dose) to -2.8 log (400mg dose) and -2.4 log (for both doses), respectively, comparable with other capsid inhibitors currently in development.

- No SAEs were observed in CHB subjects (N= 24).

- Four CHB subjects (two in each of the cohorts) experienced Grade 4 alanine aminotransferase (ALT) flares which returned to baseline levels upon AB-506 discontinuation or completion of the 28-day treatment period. Aspartate aminotransferase (AST) values were also elevated to a lesser degree, however, none of the subjects met the criteria for drug induced liver injury (DILI) as bilirubin values and liver synthetic function remained normal. All four ALT flares occurred after the subjects experienced a >2 log decline in HBV DNA from baseline.

  - We believe at least one of the ALT flare cases was immune-mediated and beneficial, as one subject in the 400 mg cohort who experienced a Grade 4 ALT flare also had notable declines in HBsAg and HBeAg of -1.4 log and -2.0 log, respectively, by Day 100 following AB-506 discontinuation. This subject was immediately put on nucleoside analog therapy after AB-506 discontinuation per investigator’s decision. In addition, serum-based cytokine analysis of this subject showed an abrupt increase in IFN-gamma at the time of the flare, suggesting an immune-mediated response. For the other 3 subjects we continue to investigate the nature of the flares.

  - Of these four subjects, two (one in each cohort) were asymptomatic, the other two (one in each cohort) had various mild to moderate AEs at the time of their flares, one with mild heaviness in head, flatulence, discomfort and moderate fatigue, one with mild rash (knees, ankles, fingers and buttock).

- Two subjects in the 160 mg cohort experienced Grade 2 ALT flares. Both were asymptomatic and returned to baseline levels upon completing the 28-day treatment period.

“While ALT flares have occurred with other capsid inhibitors, thus far none have appeared to be associated with meaningful declines in HBsAg,” said Dr. Gaston Picchio, Chief Development Officer of Arbutus Biopharma. “We believe this could represent the first case of an immune-mediated capsid inhibitor-induced ALT flare associated with significant and sustained reductions in both HBsAg and HBeAg.”

Dr. Picchio added, “To date, all capsid inhibitor studies done in healthy subjects have been limited to a maximum of 14 days of dosing. In the second half of 2019 we intend to initiate a healthy subjects study testing 28 days of dosing. An absence of flares in this study, if observed, should help us better understand the nature of the ALT flares observed in the CHB cohorts.”

Next Steps

A detailed analysis of these Phase 1a/1b preliminary results, including a complete characterization of the ALT flare cases and preliminary results from

the new 28 day study in healthy subjects, will be submitted for presentation at a scientific meeting later this year.

About the AB-506 Phase 1a/1b Clinical Trial

AB-506-001 is a double-blind, randomized, placebo controlled, single and multiple dose clinical trial evaluating the safety, tolerability and pharmacokinetics of AB-506, an oral class II capsid inhibitor, in healthy subjects and HBV-DNA positive subjects with chronic HBV infection. The healthy subject portion of the clinical trial and two cohorts of CHB subjects have been completed. The healthy subject portion consisted of a single ascending dose (SAD) part in which subjects were randomized 6:2 (active: placebo), n=21, to receive AB-506 doses ranging from 30-1000 mg, including investigation of food effect, and a multiple dose (MD) part in which subjects (randomized 10:2, n=12) received 400 mg of AB-506 once daily for 10 days. The third part of the study is enrolling HBV DNA+, HBeAg-positive or -negative CHB subjects (randomized 10:2; n=12 per cohort) at different doses of AB-506, with or without a nucleoside analog, once daily for 28 days. Dosing of additional cohorts is planned.

About AB-506

AB-506 is an oral HBV capsid inhibitor. HBV core protein assembles into a capsid structure, which is required for viral replication. The current standard-of-care therapy for HBV, primarily nucleoside analogues that work by stopping the viral polymerase, significantly reduce virus replication, but not completely. Capsid inhibitors inhibit replication by preventing the assembly of functional viral capsids and also by inhibiting the uncoating step of the viral life cycle thus reducing the formation of new covalently closed circular DNA (cccDNA), the viral reservoir which resides in the cell nucleus.

Conference Call Today

Arbutus will hold a conference call and webcast today, Monday, July 15, 2019 at 4:45 PM Eastern Time, to discuss the preliminary Phase 1a/1b clinical trial results for AB-506. You can access a live webcast of the call through the Investors section of Arbutus' website at www.arbutusbio.com. Alternatively, you can dial (866) 393-1607 or (914) 495-8556 and reference conference ID 8499742.

An archived webcast will be available on the Arbutus website after the event. Alternatively, you may access a replay of the conference call by calling (855) 859-2056 or (404) 537-3406, and reference conference ID 8499742.

About Arbutus

Arbutus Biopharma Corporation is a publicly traded (Nasdaq: ABUS) biopharmaceutical company dedicated to discovering, developing and commercializing a cure for patients suffering from chronic Hepatitis B infection. Arbutus is developing multiple drug candidates, each of which have the potential to improve upon the standard of care and contribute to a curative combination regimen. For more information, visit www.arbutusbio.com.

Forward-Looking Statements and Information

This press release contains forward-looking statements within the meaning of the Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, and forward-looking information within the meaning of Canadian securities laws (collectively, “forward-looking statements”). Forward-looking statements in this press release include statements about the safety and efficacy of AB-506; the timing and expectations regarding Arbutus’ ongoing clinical trials; the potential for AB-506 to contribute to the inhibition of HBV replication as part of a combination regime; and the potential for our drug candidates to improve upon the standard of care and contribute to a curative combination regime.

With respect to the forward-looking statements contained in this press release, Arbutus has made numerous assumptions regarding, among other things: the effectiveness and timeliness of preclinical and clinical trials, and the usefulness of the data; the availability and timing of data from clinical trials; and the adequacy of any clinical models. While Arbutus considers these assumptions to be reasonable, these assumptions are inherently subject to significant business, economic, competitive, market and social uncertainties and contingencies.

Additionally, there are known and unknown risk factors which could cause Arbutus' actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements contained herein. Known risk factors include, among others: anticipated clinical trials may be more costly or take longer to complete than anticipated, and may never be initiated or completed, or may not generate results that warrant future development of the tested drug candidate; the possibility that interim data of the Phase 1a/1b clinical trial are not indicative of final data from all patients in the clinical trial and final data may not be positive with regard to the safety or efficacy of AB-506; Arbutus may not receive the necessary regulatory approvals for the clinical development of Arbutus' products; economic and market conditions may worsen; and market shifts may require a change in strategic focus.

A more complete discussion of the risks and uncertainties facing Arbutus appears in Arbutus' Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and periodic and continuous disclosure filings, which are available at www.sedar.com and at www.sec.gov. All forward-looking statements herein are qualified in their entirety by this cautionary statement, and Arbutus disclaims any obligation to revise or update any such forward-looking statements or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments, except as required by law.

Contact Information

Investors
William H. Collier
President and CEO
Phone: 604-419-3200
Email: ir@arbutusbio.com

Media
Pam Murphy
Investor Relations Consultant
Phone: 604-419-3200
Email: ir@arbutusbio.com

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