



Arbutus Presents HBV Data at 2017 AASLD Liver Meeting

October 24, 2017

*Phase 2 ARB-1467 Combination Study Starting in 4Q17
Expected IND-filings in 2018 for Two New Oral Compounds*

VANCOUVER, British Columbia and WARMINSTER, Pa., Oct. 24, 2017 (GLOBE NEWSWIRE) -- Arbutus Biopharma Corporation (Nasdaq:ABUS), an industry-leading hepatitis B Virus (HBV) therapeutic solutions company, today presented results from clinical and preclinical studies of HBV therapeutic agents in two oral presentations and five poster presentations, including a late breaker poster presentation, at The Liver Meeting 2017 organized by the American Association for the Study of Liver Diseases (AASLD) held on October 20 – 24, 2017 in Washington, DC. These presentations feature multiple Arbutus pipeline programs that highlight the potential of its product candidates and the breadth of its portfolio being advanced to improve current cure rates in chronic HBV.

"The number of accepted abstracts and scope of data we presented at this year's AASLD conference reflect the breadth and quality of our HBV R&D pipeline," said Dr. Mark J. Murray, Arbutus' President and CEO. "These data reveal that ARB-1467, our LNP siRNA-based agent, drove significant reductions in serum HBV surface antigen (HBsAg) levels, which has informed the design of the longer duration combination study with ARB-1467, tenofovir, and pegylated interferon that will be initiated later this year. We are excited to commence this innovative proof-of-concept combination study, which has the potential to lead to HBsAg loss in some patients. Other presentations highlighted our very promising next-generation capsid inhibitor and HBV RNA destabilizer compounds that could be important contributors to future curative combination treatment regimens. We look forward to sharing more clinical data on these programs as we move into the next phases of these studies."

Presentations Include:

Poster #LB-17: Bi-weekly Dosing of ARB-1467 LNP siRNA in HBeAg Negative, Virologically Suppressed Patients with Chronic HBV Infection Leads to Deeper Declines in HBsAg and Potential Association with IL28b by *Dr. Kosh Agarwal, MD, Hepatologist and Transplant Physician, Institute of Liver Studies, King's College Hospital, London, UK*

- ***Bi-weekly dosing with ARB-1467 results in very low absolute levels of HBsAg in 5/7 patients after 5 bi-weekly doses***

ARB-1467 is Arbutus' LNP siRNA asset that inhibits HBV replication, reduces all HBV transcripts, and lowers all HBV antigens. Preliminary results from the ARB-1467 Phase II study in which 8 weeks of bi-weekly dosing with ARB-1467 are compared to 3 monthly doses in HBeAg negative subjects. All treated subjects experienced a reduction in HBsAg from baseline. Greater HBsAg reductions were observed with more frequent dosing (maximum individual decline 2.7 log IU/mL). Seven of eleven (64%) evaluable subjects receiving bi-weekly doses had a decline of $\geq 1 \log_{10}$ HBsAg, reaching ≤ 1000 IU/mL during the first 10 weeks of treatment. Five of these seven (71%) subjects reached HBsAg values < 50 IU/mL by 6 weeks. Baseline HBsAg and IL28b genotype CC were significantly associated with the degree of response. Treatment with ARB-1467 was generally well tolerated.

Poster #929: "In Vivo Study of a LNP siRNA Investigational Agent Applied Sequentially with Immunomodulatory Treatments for Chronic Hepatitis B Infection" by *Amy Lee, Senior Director, Research*

- ***Combination of HBsAg reduction and immune boosting therapies leads to off-treatment control in preclinical models***

In a preclinical animal model of chronic HBV infection, we examined drug combinations of one of our antigen reducing LNP siRNA agents with immune boosting treatments to invigorate host immune responses to HBV and facilitate long-lasting control of the virus even after cessation of treatment. Combination of LNP siRNA treatment with checkpoint blockade resulted in reduction of serum HBsAg to low levels (0.2-8 IU/mL), stimulation of HBV-specific immune cells, and increased production of anti-HBs antibody. Off-treatment viral control was achieved upon further addition of a HBV vaccine in this preclinical model. These data are consistent with the hypothesis that management of HBsAg is a critical element in the development of curative therapy. Antigen reduction, in combination with agents that boost immune reactivation applied in a specific sequence, could improve clinical treatment efficacy.

Poster #953: "Antiviral Characterization of a Next Generation Chemical Series of HBV Capsid Inhibitors In Vitro and In Vivo" by *Michael J. Sofia, Chief Scientific Officer*

- ***Next-generation HBV capsid inhibitor with improved potency and pharmacokinetics (PK) expands Arbutus' portfolio of antivirals agents***

AB-506 is Arbutus' next-generation, highly selective HBV capsid inhibitor from a novel chemical series, that exhibits favorable drug-like properties and demonstrates potent inhibition of HBV replication in vitro and in vivo. In an HBV cell culture model, AB-506 treatment resulted in empty capsid formation devoid of the viral genome. High resolution X-ray structure shows that AB-506 binds to the HBV core protein at the dimer:dimer interface and provides a rationale for improved potency through increased binding interaction with its target. Experimentally, this improved binding interaction conferred increased thermal stability to core protein indicating improved target engagement compared to first generation capsid inhibitors. Dosing studies performed in multiple species suggest potential for once a day oral administration where significant liver concentrations of AB-506 were achieved. AB-506 is being evaluated for advancement into clinical development and is expected to be the subject of an IND (or equivalent) filing around mid-year 2018.

Poster #917: “Single Dose Safety, Tolerability, and Pharmacokinetics of AB-423 in Healthy Volunteers from the ongoing Single and Multiple Ascending Dose Study AB-423-001” by Timothy Eley, Senior Director, Clinical Pharmacology

- **AB-423 to advance into multi ascending dose (MAD) study in HBV patients after favorable safety and PK results in healthy volunteers**

AB-423 is a potent, orally administered, highly selective HBV capsid inhibitor, which is being developed to treat chronic HBV infection. An interim analysis of single dose cohorts from AB-423-001 demonstrated that AB-423 was readily absorbed post-dose with maximum concentrations occurring approximately 2-2.5 hours post dose and increases in concentrations over time largely proportional with changes in dose from 12.5 to 800mg single doses. Three active major metabolites were present in concentrations sufficient to contribute to antiviral response in the clinic and the ratio of concentration of each metabolite relative to AB-423 was largely consistent across dose panels. AB-423 has been generally well-tolerated with safety data unremarkable following single doses up to 800mg. Adverse events (AEs) were mostly mild, all resolved prior to study discharge and there were no dose related trends in AEs. There were no serious adverse events, deaths, or discontinuations and no clinically significant changes in vital signs, ECGs or physical exams. In summary, AB-423's favorable safety and PK profile following single doses supports further evaluation of multiple-dose administration of AB-423.

Poster #923: “Identification and Characterization of AB-452, a Potent Small Molecule HBV RNA Destabilizer In Vitro and In Vivo” by Dimitar Gotchev, Senior Principal Scientist, Chemistry

- **A novel anti-viral agent targeting all HBV RNAs is added to Arbutus' expanding pipeline of HBV therapeutic agents**

AB-452 is a novel, orally-bioavailable, small-molecule HBV RNA destabilizer that has broad genotype coverage. Unlike nucleos(t)ides, AB-452 not only inhibits HBV DNA, but also affects all stages of the HBV lifecycle such as RNA, total amount of protein, capsid DNA, DNA replication, and S protein. The compound is HBV specific and shows synergistic effects when combined with two of Arbutus' proprietary HBV LNP siRNA agents in vitro. AB-452 also works in vivo. In the mouse AAV model, twice-a-day oral administration of AB-452 results in up to 1.4 log₁₀ reduction of serum HBsAg in a dose dependent manner and correlates well with liver HBV RNA levels. AB-452 has the potential for once daily, oral dosing and is being evaluated for advancement into clinical development, expecting to be the subject of an IND (or equivalent) filing around mid-year 2018.

Oral Presentation #42: “Pharmacokinetics and Exploratory Exposure-Response of siRNAs Administered Monthly as ARB-001467 (ARB-1467) in a Phase 2a Study in HBeAg Positive and Negative Virally Suppressed Subjects with Chronic Hepatitis B” by Timothy Eley, Senior Director, Clinical Pharmacology

- **Relationship between serum concentrations of ARB-1467 and HBsAg reduction informs selection of optimized treatment of ARB-1467**

ARB-1467 is a novel LNP siRNA agent designed to inhibit viral replication, reduce all HBV transcripts, and lower all viral antigens. Evaluating the concentrations in blood/plasma over time of the siRNA in the monthly dosing cohorts from ARB-1467-002 and exploring relationships between those data and reduction in HBsAg in treated patients informed the selection of optimized treatment. We found that on average both increased with increasing dose in HBeAg- patients from 0.2mg/kg vs. 0.4mg/kg, but individual response to treatment was not well predicted by concentrations in blood/plasma over time. Based on the results of this initial analysis, patient and disease specific factors affecting response require further evaluation and future assessments, such as this, should incorporate any identified confounding factors. Additionally, evaluating different measures of response to ARB-1467 treatment is warranted.

Oral Presentation #40: “HBcrAg, HBV-RNA declines in A Phase 2a Study Evaluating the Multi-dose Activity of ARB-1467 in HBeAg-Positive and Negative Virally Suppressed Subjects with Hepatitis B” by Dr. Kosh Agarwal, MD, Hepatologist and Transplant Physician, Institute of Liver Studies, King's College Hospital, London, UK

- **Measurement of HBcrAg and HBV-RNA contributes to a greater understanding of the utility of HBV markers**

Hepatitis B core-related antigen (HBcrAg) was evaluated for monitoring the response to novel chronic HBV treatment as HBcrAg and HBV-RNA have been suggested as additional markers of HBV infection. Using Arbutus' LNP siRNA agent, ARB-1467, treatment was generally well tolerated and all subjects receiving ARB-1467 experienced a reduction in HBV surface antigen (HBsAg) from baseline. Greater HBsAg reductions were observed with more frequent dosing (bi-weekly) and at the higher dose (0.4 mg/kg). On treatment reductions in HBcrAg and HBV-RNA were observed in some individual patients but overall there was no apparent correlation between declines in HBV-RNA or HBcrAg and declines in HBsAg. Further evaluation of the utility of these markers across different populations and treatment durations is required to determinate the utility of HBcrAg for monitoring the response to novel chronic HBV treatment.

Posters and Presentations

AASLD posters and presentations are available by visiting the Investor section of Arbutus' website at www.arbutusbio.com and selecting Events and Presentations.

About Arbutus Biopharma

Arbutus Biopharma Corporation is a biopharmaceutical company dedicated to discovering, developing and commercializing a cure for patients suffering from chronic HBV infection. Arbutus is headquartered in Vancouver, BC, and has facilities in Warminster, PA. For more information, please 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 two oral presentations and five poster presentations at The Liver Meeting 2017; the potential for Arbutus' capsid inhibitor and HBV RNA destabilizer compounds to become important contributors to future

curative combination treatment regimens; potential advancement of AB-506 into clinical development and an IND (or equivalent) filing around mid-year 2018; potential advancement of AB-452 into clinical development and an IND (or equivalent) filing around mid-year 2018; and discovering, developing and commercializing a cure for patients suffering from chronic HBV infection.

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 clinical trials, and the usefulness of the data; the continued demand for Arbutus' assets; and the stability of economic and market conditions. 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; 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 and Arbutus' 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.

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Source: Arbutus Biopharma Corporation