



## Arbutus Presents Complementary Results From Preclinical Combination Studies of HBV Therapeutic Candidates at EASL 2018

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*Capsid inhibitor with HBV RNA Destabilizer Demonstrate Complementary Efficacy Results  
Subcutaneous RNAi Agent Demonstrates Durable HBsAg Reduction Following a Single Dose*

VANCOUVER, British Columbia and WARMINSTER, Pa., April 12, 2018 (GLOBE NEWSWIRE) -- Arbutus Biopharma Corporation (Nasdaq:ABUS), an industry-leading Hepatitis B Virus (HBV) therapeutic solutions company, today made two presentations supporting our drug combination approach at the 53rd Annual International Liver Congress of the European Association for the Study of the Liver (EASL) in Paris, France.

"Data presented at EASL 2018 is an endorsement of our combination strategy and the breadth and quality of our therapeutic candidates," said Dr. Mark J. Murray, Arbutus' President and CEO. "Our next-generation capsid inhibitor AB-506 and novel HBV RNA destabilizer AB-452 were studied in combination with our LNP RNAi (siRNA) candidate ARB-1467 and approved HBV therapies. In these studies, AB-506 and AB-452 exhibited distinct but complementary antiviral activities, supportive of inclusion in clinical combination regimens. Separately, compared to earlier RNAi therapies for HBV, more durable antiviral activity was achieved in vivo with AB-729, our GalNAc-enabled, subcutaneously delivered, RNAi candidate. In totality, these data support further clinical evaluation of our promising new agents and development of a proprietary drug combination for treatment of chronic HBV."

### Presentations Include:

**Oral Presentation #3503: "Preclinical Antiviral Drug Combination Studies Utilizing Novel Orally Bioavailable Investigational Agents for Chronic Hepatitis B Infection: AB-506, a Next Generation HBV Capsid Inhibitor, and AB-452, an HBV RNA Destabilizer"** by Rene Rijnbrand, VP Head of Biology at Arbutus Biopharma

- ***When combined, our capsid inhibitor AB-506 and HBV RNA destabilizer AB-452 show distinct but mechanistically compatible antiviral activities that suggest feasibility of inclusion in a clinical combination regimen.***

Summary: We evaluated the anti-HBV activities of two novel orally administered agents, an HBV capsid inhibitor AB-506 and an HBV RNA destabilizer AB-452, in combination with approved standard of care (SOC) therapies: nucleos(t)ide analogs (NA), entecavir (ETV), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), and our lead RNAi agent, ARB-1467. The in vitro dual combinations of AB-506 or AB-452 with approved NAs or ARB-1467 ranged from additive to moderately synergistic at reducing HBV rcDNA and HBsAg levels with no significant effects on cell viability. After a once-daily 7-day oral treatment period in HDI HBV mice, dual combinations of AB-506+AB-452, AB-506+TDF, and AB-452+TDF demonstrated a strong antiviral activity with mean 1.4, 1.9, and 2.2 log reductions in serum HBV DNA vs. the vehicle control, respectively, whereas the triple combination effected larger serum HBV DNA reductions, 2.8 log vs. the vehicle control. All AB-506 and AB-452 treated groups demonstrated reductions in liver HBV DNA, with negligible reduction observed with TDF alone. Serum HBsAg reduction was detected in AB-452 treated groups, and when combined with AB-506 and/or TDF there was no adverse effect on the ability of AB-452 to reduce HBsAg. These preclinical investigations suggest that these agents when combined have distinct but mechanistically compatible antiviral activities and may feasibly be used in future combination therapeutic regimens.

**Oral Presentation #2646: "Durable Inhibition of Hepatitis B Virus Replication and Antigenemia Using Subcutaneously Administered siRNA Agent AB-729 in Preclinical Models"** by Amy Lee, Senior Director, Research at Arbutus Biopharma

- ***GalNAc siRNA offers the potential for subcutaneous delivery of siRNA therapies and showed more durable in vivo preclinical activity compared to earlier-generation siRNA agents for HBV.***

Summary: AB-729 is a next-generation siRNA therapeutic targeted to hepatocytes using our novel covalently conjugated N-acetylgalactosamine (GalNAc) delivery technology. This is a promising new subcutaneously administered agent, which acts on multiple HBV viral transcripts, enabling inhibition of viral replication and suppression of all viral antigens. AB-729 showed more durable in vivo preclinical activity than earlier-generation siRNA agents for the treatment of chronic HBV infection. In comparison to lipid nanoparticle (LNP)-mediated intravenous delivery, GalNAc-conjugated subcutaneous delivery of the same reference siRNA required a 10-fold greater dose to achieve similar mean maximum inhibition of serum HBsAg in AAV-HBV mice. However, HBsAg suppression in the LNP treatment group had fully resolved by Week 4 whereas the GalNAc treatment group nadir persisted from Week 2 through to Week 6. One dose of AB-729 was sufficient to achieve mean maximum HBsAg reductions of 1.4, 2.8 and 3.9 log<sub>10</sub> at 1, 3 and 9 mg/kg, respectively, in AAV-HBV mice with baseline serum HBsAg 3.6 log<sub>10</sub> IU/mL. In vivo AB-729 suppression of HBsAg was also highly durable, with 83%, 89% and 99%, respectively, of the mean maximal effect remaining at Week 10 after a single dose.

### Presentations

EASL 2018 presentations are available by visiting the Investor section of Arbutus' website at [www.arbutusbio.com](http://www.arbutusbio.com) and selecting Events and Presentations.

### 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 (HBV) infection. Arbutus is developing multiple drug candidates, each of which

have the potential to improve upon the standard of care (SOC) and contribute to a curative combination regimen to improve patient outcomes and deliver a potential cure for HBV. For more information, visit [www.arbutusbio.com](http://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 possible inclusion of AB-506 and AB-452 in future drug combination regimens; further clinical evaluation of our clinical assets, including AB-506, AB-452 and AB-729, and eventual testing of a proprietary combination; the potential for subcutaneous delivery of siRNA therapies; 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 <http://www.sedar.com> and at [www.sec.gov](http://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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