Arbutus Presents New Data on AB-729, AB-836 and AB-101 at the EASL International Liver Congress™ 2022 and Provides AB-836 Clinical Update

June 25, 2022

AB-729, our RNAi therapeutic, provided robust and comparable HBsAg declines in both HBeAg+ and HBeAg- patients

50% (16 out of 32) of patients maintained HBsAg levels below 100 IU/mL 24 weeks after their last AB-729 dose

In the first five patients who discontinued both AB-729 and NA therapy after meeting stopping criteria, there has been no evidence of virologic or clinical relapse in 8-24 weeks of follow-up

Preliminary data to date have shown that AB-729 remains generally safe and well-tolerated after completing dosing in 41 patients

AB-729 continues to restore HBV-specific T-cells and decrease exhausted T-cells

AB-836, our oral capsid inhibitor, dosed at 100mg or 200mg once daily for 28 days, achieved mean declines in HBV DNA of 3.04 and 3.55 log_{10}, respectively, however safety findings warrant further evaluation in healthy volunteers

AB-101, our oral PD-L1 inhibitor, mediates activation and reinvigoration of HBV-specific T-cells from chronic hepatitis B patients in a pre-clinical model

Conference Call and Webcast Scheduled for 8:00 AM ET, Monday, June 27, 2022

WARMINSTER, Pa., June 25, 2022 (GLOBE NEWSWIRE) -- Arbutus Biopharma Corporation (Nasdaq: ABUS), a clinical-stage biopharmaceutical company leveraging its extensive virology expertise to develop novel therapeutics that target specific viral diseases, today announced the presentation of new clinical and pre-clinical data from its proprietary compounds at the European Association for the Study of the Liver (EASL) International Liver Congress™ (ILC).

The new clinical data for AB-729, our RNAi therapeutic, continues to support its development as a potential cornerstone agent for the treatment of chronic hepatitis B (cHBV) infection. In addition, when AB-729 and nucleos(t)ide analogues (NA) were discontinued in the first five patients who met stopping criteria and consented, there was no evidence of virologic or clinical relapse in at least 8-24 weeks of follow-up, which may lead to a functional cure.

AB-836, our oral capsid inhibitor, demonstrated robust antiviral activity, however, two patients in the 200 mg cohort experienced alanine aminotransferase (ALT) elevations. Based on these observations along with potentially correlated immunological findings, we plan to conduct a Phase 1 clinical trial in healthy volunteers before progressing this program.

William Collier, President and Chief Executive Officer of Arbutus, commented, “Our comprehensive AB-729 data package that has been accepted for presentation at EASL, is indicative of the continued impressive clinical safety and efficacy profile seen with AB-729 in 41 patients. Our clinical team has conducted a thorough evaluation of this compound in cHBV patients with different characteristics to identify an adequate dose and dosing schedule to move into our ongoing Phase 2a clinical trials which will support our Phase 2b clinical program. We believe that AB-729 is capable of being a cornerstone agent in the treatment regimen to provide a functional cure for patients with cHBV.”

AB-729-001 Clinical Data Poster Presentations

Professor Man-Fung Yuen, D.Sc., M.D., Ph.D., Deputy Head of Department, Chief of Division of Gastroenterology and Hepatology, Master of Lap Chee, University of Hong Kong, and lead investigator of AB-729-001 clinical trial, presented a poster titled, “Continued suppression of viral markers observed following discontinuation of nucleos(t)ide analogue therapy in chronic hepatitis B subjects with low hepatitis B surface antigen levels after 48 weeks of treatment with AB-729”.

This presentation focused on the preliminary safety and virology data from those patients in part 3 of the AB-729-001 clinical trial who completed treatment with AB-729 and, after meeting the protocol-defined criteria, elected to stop their NA-therapy (n=9). Prof. Yuen reported on the first five of the nine patients that had between 8 and 24 weeks of data following discontinuation of all treatment.

The mean HBsAg for the five patients at baseline was 2887 IU/mL (range 1392-6765) compared to 69 IU/mL (range 4.58-150.1) at the last visit after discontinuing all treatment. All five patients remain off all treatment, and all have HBsAg levels below pre-baseline levels. None of the patients have met clinical or virologic relapse criteria. There were no adverse events (AEs) reported, no ALT elevations observed, and HBV DNA levels remain either less than the LLOQ (lower limit of quantification) or have transiently risen and subsequently decreased without intervention.

HBV Parameter	Pt. 46	Pt. 51	Pt. 52	Pt. 53	Pt. 61
HBsAg (IU/mL)					
Study Day 1	1392	6765	1888	2368	2021
Week 48/EOT	5	29.61	9.54	22.76	1.64
Last Visit prior to NA d/c	10.53	64.9	3.95	69.06	3.99
Last available post-NA d/c	41.22	150.1	10.97	138.9	4.58

HBcrAg (log U/mL)					
Study Day 1	3.8	<3.0	3.2	4.2	3.7
Week 48/EOT	3.4	<3.0	3	4.4	3.4
Last Visit prior to NA d/c	3.4	<3.0	3	4.5	3.5
Last available post-NA d/c	3.4	<3.0	3.1	4.5	3.6
HBV RNA (log_{10} U/mL)					
Study Day 1	2.07	TND	<LLOQ	<LLOQ	N/A
Week 48/EOT	TND	TND	0.7	TND	TND
Last Visit prior to NA d/c	1.29	1.07	1.2	TND	1.43
Last available post-NA d/c	1.16	1.31	1.36	1.08	1.09

Dr. Gaston Picchio, Chief Development Officer of Arbutus Biopharma, stated: "I am most excited with the data showing that after discontinuing treatment with AB-729 and NA-therapy, patients maintained a sustained reduction in HBsAg while avoiding an HBV DNA relapse. This degree of virologic control in the absence of any therapies could be in part explained by our findings showing evidence of an increase in HBV-specific T-cell proliferation *in vitro* using peripheral blood mononuclear cells from patients dosed with AB-729."

"The additional data from the AB-729-001 clinical trial are extremely impressive," stated Prof. Yuen. "To see patients maintain a sustained control of both HBsAg and HBV DNA after stopping all treatments is quite encouraging, although additional follow up is necessary to confirm these findings. We are continuing to follow these patients for one-year post discontinuation of all medications, to monitor for partial or functional cure."

Prof. Yuen also presented data from a poster titled, "Long-term suppression maintained after cessation of AB-729 treatment and comparable on-treatment response observed in HBeAg+ subjects".

With dosing complete in all six cohorts of patients (n=41), Prof. Yuen presented the following new data from Cohort K (n=7) which included HBeAg+ patients only:

- All seven patients reached HBsAg levels <100 IU/ml during AB-729 treatment or follow-up.
- Two patients reached HBsAg levels <LLOQ at one or more visits.
- The mean (SE) log_{10} change from baseline in HBeAg at end of treatment was -0.94(0.25) IU/mL.

In addition, Prof. Yuen presented follow-up data on Cohort G, which included HBV DNA+ patients who began treatment with tenofovir disoproxil fumarate concurrently with AB-729, and Cohorts E, F, I and J, which enrolled HBeAg- and HBV DNA- patients and evaluated different doses and dosing intervals. The reported data for these patients showed:

- 26 of 34 patients had HBsAg <100 IU/mL at some point during the trial.
- Most patients had a robust decline in HBsAg that was maintained well after cessation of AB-729 treatment, mean log change from baseline to 24 weeks post last dose was approximately -1.5 log_{10} across cohorts.
- Repeat dosing of AB-729 continues to be generally safe and well-tolerated with only transient Grade 1 or 2 ALT elevations.

Prof. Yuen continued, "This data shows that HBsAg responses with AB-729 are robust across all cohorts regardless of dose, dosing interval, HBeAg or HBV DNA status. In addition, the vast majority of patients reached HBsAg levels of less than 100 IU/mL, which is a clinically relevant threshold that could inform when to stop all therapies. With the encouraging safety and tolerability profile of AB-729, I look forward to continuing to develop this promising compound."

AB-836 Clinical Data Presentation

Prof. Edward Gane, University of Auckland, New Zealand Liver Transplant Unit, Auckland, New Zealand, presented the full data from this trial in a poster titled, "Safety, tolerability, pharmacokinetics, and antiviral activity of the 3rd generation capsid inhibitor AB-836 in healthy subjects and subjects with chronic hepatitis B".

AB-836-001 is a Phase 1a/1b clinical trial evaluating the safety and tolerability of multiple doses of AB-836 in patients with cHBV infection. Data from part 3 of the trial showed that the 100mg and 200mg doses of AB-836 provided potent inhibition of HBV replication with mean declines in HBV DNA at Day 28 of 3.04 and 3.55 log_{10} IU/mL, respectively. From a safety standpoint, there were no deaths or SAEs observed. Two HBeAg+ patients in the 100mg dose cohort had transient Grade 3 ALT elevations that resolved with continued dosing and were not considered treatment emergent adverse events (TEAEs). Two patients in the 200mg cohort had Grade 3 and Grade 4 ALT elevations on the last day of dosing (Day 28) that returned to baseline during follow up which were reported as TEAEs. The Grade 3 and Grade 4 ALT elevations seen in the 200 mg cohort were accompanied by serum IP-10 increases, a cytokine previously described to be associated with potential liver toxicity in the capsid inhibitor space. All patients with ALT elevations were asymptomatic and none had changes in bilirubin or met drug-induced liver injury (DILI) criteria. There were no other clinically significant lab abnormalities, ECG or vital sign changes observed.

Dr. Gaston Picchio, Chief Development Officer of Arbutus, commented, "I am impressed with the potency of AB-836, but disappointed with the safety signal seen in the 200mg cohort, especially since AB-836 demonstrated an encouraging safety profile pre-clinically. While the Grade 3 and Grade 4 ALT elevations resolved during follow-up and were not associated with clinical symptoms, they were accompanied by an increase in IP-10, an exploratory and hence not a definitive biomarker which we had previously observed in cases of liver toxicity associated with capsid inhibitors, and so we have decided, in the interest of patient safety, that we need to conduct an additional Phase 1 trial in healthy volunteers. We believe data from this additional study will help to determine whether or not these ALT elevations could be the result of liver toxicity. We will provide an update with respect to the status and timing of this clinical trial at a later date."

AB-101 Preclinical Poster Presentation

Dr. Emily Thi presented data from a poster titled, "Preclinical activity of small-molecule oral PD-L1 checkpoint inhibitors capable of reinvigorating T cell

responses from chronic hepatitis B patients."

The purpose of this study was to assess the preclinical activity of AB-101 and the compound's ability to reinvigorate patient HBV-specific T-cells. Studies were conducted using a transgenic MC38 tumor mouse model and peripheral blood mononuclear cells (PBMCs) from cHBV patients. The data presented showed that once daily oral administration of AB-101 resulted in profound tumor reduction that was associated with T-cell activation. In addition, AB-101 activates and reinvigorates HBV-specific T-cells. This favorable preclinical profile supports further development of AB-101 as a therapeutic modality for cHBV treatment. AB-101 is currently undergoing IND-enabling activities.

All of the posters that were presented at EASL 2022 can be accessed through the Investors section of Arbutus' website under Events & Presentations at www.arbutusbio.com.

Conference Call and Webcast:
Arbutus will hold a conference call and webcast on Monday, June 27, 2022, at 8:00 AM Eastern Time to summarize the data presented at EASL. You can access a live webcast of the call, which will include presentation slides, 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 7014417.

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 7014417.

About AB-729

AB-729 is an RNA interference (RNAi) therapeutic specifically designed to reduce all HBV viral proteins and antigens, including hepatitis B surface antigen, which is thought to be a key prerequisite to enable reawakening of a patient's immune system to respond to the virus. AB-729 targets hepatocytes using Arbutus' novel covalently conjugated *N*-Acetylgalactosamine (GalNAc) delivery technology that enables subcutaneous delivery. Clinical data generated thus far has shown single- and multi-doses of AB-729 to be generally safe and well-tolerated while providing meaningful reductions in hepatitis B surface antigen and hepatitis B DNA. AB-729 is currently in multiple Phase 2a clinical trials.

About AB-836

AB-836 is a next generation oral hepatitis B virus (HBV) capsid inhibitor that interacts with HBV core protein, which in turn is required for viral replication. The current standard-of-care therapy for HBV is primarily nucleos(t)ide analogues that inhibit the viral polymerase and significantly reduce, but do not eliminate viral replication. AB-836 in combination with nucleos(t)ide analogues is designed to completely eliminate viral replication in infected cells by preventing the assembly of functional viral capsids. In addition, AB-836 has been shown to inhibit the replenishment of covalently closed circular DNA (cccDNA), the viral genetic reservoir which the virus needs to replicate itself.

About AB-101

Immune checkpoints such as PD-1/PD-L1 play an important role in the induction and maintenance of immune tolerance and in T-cell activation. We have identified a class of small molecule oral PD-L1 inhibitors that we believe will allow for controlled checkpoint blockade, enable oral dosing, and mitigate systemic safety issues typically seen with checkpoint antibody therapies. Our lead oral PD-L1 inhibitor candidate, AB-101, is currently in IND-enabling studies. We believe AB-101 has the potential to be used in combination with other approved and investigational agents for our mission to achieve a functional cure for HBV chronically infected patients. We are also exploring oncology applications for our internal PD-L1 portfolio.

About HBV

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). HBV can cause chronic infection which leads to a higher risk of death from cirrhosis and liver cancer. Chronic HBV infection represents a significant unmet medical need. The World Health Organization estimates that over 290 million people worldwide suffer from chronic HBV infection, while other estimates indicate that approximately 2.4 million people in the United States suffer from chronic HBV infection. Approximately 820,000 people die every year from complications related to chronic HBV infection despite the availability of effective vaccines and current treatment options.

About Arbutus

Arbutus Biopharma Corporation (Nasdaq: ABUS) is a clinical-stage biopharmaceutical company leveraging its extensive virology expertise to develop novel therapeutics that target specific viral diseases. Our current focus areas include Hepatitis B virus (HBV), SARS-CoV-2, and other coronaviruses. In HBV, we are developing a RNAi therapeutic, an oral capsid inhibitor, an oral PD-L1 inhibitor, and oral RNA destabilizer that we intend to combine with the aim of providing a functional cure for patients with chronic HBV by suppressing viral replication, reducing surface antigen and reawakening the immune system. We believe our lead compound, AB-729, is the only RNAi therapeutic with evidence of immune re-awakening. It is currently being evaluated in multiple phase 2 clinical trials. We also have an ongoing drug discovery and development program directed to identifying novel, orally active agents for treating coronavirus (including SARS-CoV-2). In addition, we are exploring oncology applications for our internal PD-L1 portfolio. 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 our future development plans for our product candidates; the expected cost, timing and results of our clinical development plans and clinical trials with respect to our product candidates; our expectations with respect to the release of data from our clinical trials and the expected timing thereof; our expectations and goals for our collaborations with third parties and any potential benefits related thereto; and the potential for our product candidates to achieve success in clinical trials.

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 studies and clinical trials, and the usefulness of the data; the timeliness of regulatory approvals; 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, including uncertainties and contingencies related to the ongoing COVID-19 pandemic and patent litigation matters.

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 pre-clinical studies and 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 product candidate; Arbutus may elect to change its strategy regarding its product candidates and clinical development activities; Arbutus may not receive the necessary regulatory approvals for the clinical development of Arbutus' products; economic and market conditions may worsen; uncertainties associated with litigation generally and patent litigation specifically; Arbutus and its collaborators may never realize the expected benefits of the collaborations; market shifts may require a change in strategic focus; and the ongoing COVID-19 pandemic could significantly disrupt Arbutus' clinical development programs.

A more complete discussion of the risks and uncertainties facing Arbutus appears in Arbutus' Annual Report on Form 10-K, Arbutus' Quarterly Reports on Form 10-Q and Arbutus' continuous and periodic 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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