June 29, 2020

Acasti Pharma Provides Fiscal 2020 Year-End Business Update

Identifies "Triglyceride Normalization" phenomenon prior to patient randomization and treatment as likely contributor to unusually high placebo effect in TRILOGY 1

Acasti management to host conference call at1 PM ET today

LAVAL, Quebec, June 29, 2020 (GLOBE NEWSWIRE) -- Acasti Pharma Inc. ("Acasti" or the "Company") (NASDAQ: ACST – TSX-V: ACST), a biopharmaceutical innovator focused on the research, development and commercialization of its prescription drug candidate CaPre® (omega-3 phospholipid) for the treatment of severe hypertriglyceridemia (sHTG) (triglyceride blood levels from 500 mg/dL to 1500 mg/dL), today provided a business and TRILOGY Phase 3 Clinical Program update, and announced its operating and financial results for the fiscal year ended March 31, 2020.

The Company also reported a phenomenon that it refers to as "Pre-Randomization Triglyceride (TG) Normalization" that occurred between the screening and randomization periods of the study (during qualification), and prior to patients starting on drug or placebo. A summary of the post-hoc data analyses and audit findings for TRILOGY 1 can be found below, and in the Business Section of the Company's annual report on Form 10-K, which will be filed with the Securities and Exchange Commission today, and will be available on the Company's website.

Recent Corporate Highlights:

- Reported topline results for TRILOGY 1 Phase 3 trial of CaPre in January 2020
- Completed clinical site and central lab audits in fiscal Q4
- Meeting request filed with the Food and Drug Administration (FDA) to discuss TRILOGY 1 post-hoc data analysis, with request to get input on proposed revisions to the pre-specified Statistical Analysis Plan (SAP) for the TRILOGY 2 Phase 3 trial of CaPre
- Submitted briefing package with TRILOGY 1 data to FDA on April 29, 2020
- Written response received from the FDA and reported on June 19, 2020
- TRILOGY 2 topline results still expected in calendar Q3

TRILOGY 1 Post-Hoc Review Highlights:

- Rigorous post-hoc analysis of the data conducted by the Company, the academic Principal Investigator (PI) of the study, Dariush Mozaffarian M.D., Dr.P.H., and external clinical and statistical experts
- Analysis of the TRILOGY 1 data revealed a rapid, significant and sustained reduction in TG levels between screening (during qualification) and the time of patient randomization (prior to patients starting on either drug or placebo), which Acasti refers

to as “Pre-randomization TG Normalization”

- Pre-Randomization TG Normalization affected both treatment groups, but was much greater in the placebo group, resulting in a significant underestimation of the post-randomization treatment effect of the active drug, CaPre
- Company conducted post-hoc analyses of the primary endpoint using a revised, single point baseline value from Week 0 (Visit 4) which corrected for a significant amount of the pre-randomization TG reduction in subjects that were most affected by this normalization phenomenon
- Meaningful efficacy trend for CaPre observed, after correcting for the unexpectedly large placebo response in the original analysis

TRILOGY 1 Summary:

The Company released topline results from its TRILOGY 1 Phase 3 trial in January 2020, reporting a 30.5% median reduction in triglyceride levels among patients receiving CaPre at 12 weeks, and a 42.2% median reduction in triglyceride levels among patients receiving CaPre while on background statin therapy at 12 weeks. Additionally, the Company reported a 36.7% median reduction in triglyceride levels among patients receiving CaPre at 26 weeks. Despite positive results in the CaPre arm, TRILOGY 1 did not reach statistical significance due to an unusually large placebo response of 27.5% and 28.0% median reductions in triglyceride levels at 12 and 26 weeks, respectively. The safety profile of CaPre in TRILOGY 1 was similar to placebo, as there was no significant difference in treatment-related serious adverse events in the trial.

The protocol for TRILOGY 1 and 2 had input from and was approved by the FDA, and followed essentially the same standard design as has been used by all other companies running trials in sHTG. There were some slight differences in the TRILOGY 1 patient population as compared to previous studies with other omega-3 therapeutics in sHTG, but none that were believed to have contributed to the significant placebo effect. As previously reported, despite monitoring activities conducted throughout the TRILOGY 1 trial to ensure adherence to the protocol and to detect potential protocol violations, Acasti subsequently identified some unexpected and inconsistent findings that the Company believes may have negatively contributed to the unusual placebo effect. These findings were further explored via a comprehensive and rigorous post-hoc review of the data by the Company, the academic Principal Investigator (PI) of the study, Dariush Mozaffarian M.D., Dr.P.H., and external clinical and statistical experts, as well as audits of the central blood testing laboratory and certain clinical sites, which were conducted by an independent team of auditors.

This post-hoc analysis of the TRILOGY 1 data revealed a rapid, significant and sustained reduction in TG levels during the patient qualification period, which took place between screening and the time of patient randomization (that is, prior to patients starting on either drug or placebo). Acasti refers to this phenomenon as “Pre-Randomization TG Normalization.” This phenomenon, which to our knowledge has not been reported in any other TG studies, resulted in an artefactual overestimation of TG reduction in both treatment groups. However, the Pre-Randomization TG Normalization was much greater in the placebo group as compared to the CaPre group, resulting in a significant underestimation of the post-randomization treatment effect of CaPre in TRILOGY 1, and further compromising the ability of the study to detect a clinically significant drug treatment effect.

TG values are normally quite variable, and it is expected that the intra-individual TG variation in subjects on a healthy, low fat National Cholesterol Education Program (NCEP) diet may be 10% or greater (going in either direction) within a one to two week period. Thus, it is standard practice to include 2 or 3 pre-randomization TG measurements in the determination of the baseline for the calculation of the primary endpoint. The pre-randomization reduction in TGs across all subjects in TRILOGY 1 was about 20%, with 25% of all subjects experiencing a reduction equal to or greater than 38%. The median Pre-Randomization TG Normalization reached 30% or more in 12 out of 54 sites (or in 22% of all randomizing sites), in all, much greater than the 10% variation that would have been expected based on physiological variability. In addition, natural variability would have resulted in both increases and decreases in individual levels which would largely offset each other, limiting aggregate variability below 10%. The magnitude of pre-randomization reduction in TG levels seen in TRILOGY 1 indicated a largely unidirectional variability, which was not likely due solely to physiological intra-individual variation, and therefore is considered to be artefactual.

The unexpected and large magnitude of this Pre-Randomization TG Normalization phenomenon resulted in about 40% of all randomized and eligible subjects having TG levels at randomization (Visit 4 or “Week 0") that fell below the protocol specified average qualification lower threshold of ≥ 500 mg/dL for patients with sHTG.

Based on the above observations, we believe that the Pre-Randomization TG Normalization substantially impacted the outcome of TRILOGY 1, and the ability of the study to accurately determine the therapeutic impact of CaPre as measured by the pre-specified primary endpoint. Specifically, we believe that the use of an average of 3 values for the calculation of the baseline TG levels corresponding to time points during Qualification (e.g. at Week minus 2, and Week minus 1 prior to randomization), and Week 0 (at randomization), resulted in an overestimation of the TG reduction, particularly in the placebo group – with significant TG reduction occurring in many patients even before either drug or placebo were started.

The Company conducted post-hoc analyses of the primary endpoint using a revised, single point baseline value from Week 0 (Visit 4), the date of randomization, which is referred to as the “Revised Baseline.” Furthermore, only those subjects meeting the protocol-specified TG threshold of ≥ 500 mg/dL and ≤ 1500 mg/dL at Week 0 were included in this post-hoc analyses.

This revised approach for calculating the baseline TG levels corrected for a significant amount of the pre-randomization TG reduction in the subjects that were most affected by this normalization phenomenon. After patients with TG values <500 mg/dL and >1500 mg/dL on the date of randomization were removed, a total of 143 subjects remained (originally N = 242), including 42 subjects in the placebo group (originally N = 69), and 101 subjects remained in the CaPre group (originally N = 173), and were included in the post-hoc analyses representing 61% and 58% of all randomized subjects, respectively.

In this post-hoc analysis of subjects with TG levels meeting the protocol specified TG threshold of >500 mg/dL and <1500mg/dL at Week 0, subjects receiving CaPre showed a 28.1% median reduction in TG compared to a 15.4% median reduction among subjects receiving placebo after 12 weeks (this represents the primary endpoint, and a non-adjusted absolute difference of 12.7%; p = 0.29). As compared to the original analysis, the Revised Baseline attenuated the placebo response by approximately 12 percentage points (from -27.5% to -15.4%), while the response in the CaPre arm remained mostly unaffected

(reduced from -30.0% to -28.1%). After 26 weeks of double-blind treatment, the efficacy of CaPre showed good persistency of effect with a 32.6% median reduction compared with a 14.6% median reduction in the placebo group, reaching a non-adjusted difference of -18.0%, which trended toward statistical significance ($p = 0.089$). As compared to the original analysis, the Revised Baseline attenuated the placebo response at 26 weeks by approximately 13 percentage points (from -28.0% to -14.6%), while the response in the CaPre arm remained mostly unaffected (reduced from -36.7% to -32.6%). The median TG reductions seen with CaPre using this post-hoc methodology compare favorably to those of previous published studies of other FDA approved drugs for sHTG.

The subgroup of subjects with Revised Baseline TG levels above 750 mg/dL at Visit 4 (Week 0) represented 41% of the subjects retained in the post-hoc analyses. Within this group, the median TG reduction in the subjects receiving CaPre was larger as would be expected, reaching 36.3% and 43.0% at Week 12 and Week 26, respectively. In comparison, the median TG reduction for the placebo group was 11.8% at Week 12 and 14.4% at Week 26, resulting in non-adjusted differences of 24.5% and 28.6% respectively in favor of CaPre ($p = 0.22$ and 0.15, respectively).

Not surprisingly, a post-hoc power calculation revealed that these substantially smaller sample sizes resulted in reduced statistical power to detect a treatment difference of 20% as specified in the original Statistical Analysis Plan (SAP). However, the Company believes that these post-hoc results suggest clinical relevance even if statistical significance was not demonstrated, as it is plausible that the trend revealed in the post-hoc analysis may have achieved statistical significance with a larger sample size.

In summary, the post-hoc analyses of TRILOGY 1 data using the Week 0 (Visit 4) value as a Revised Baseline in subjects with TG ≥ 500 mg/dL and ≤ 1500 mg/dL at Week 0, showed a strong trend towards correcting for the unexpectedly large placebo response observed in the original analysis, without major changes in the CaPre response observed, and we believe allows for a clearer understanding of the impact on the TG primary endpoint, and the potential therapeutic effect of CaPre. However, the median difference in TG levels between CaPre and placebo from the TRILOGY 1 post-hoc analyses still fell short of reaching statistical significance at the Week 12 primary endpoint in this patient adjusted sample.

“The originally observed large reduction in TG in the placebo group was extremely unusual,” said Dr. Mozaffarian, PI of the TRILOGY study. “For unclear reasons, perhaps regression to the mean, many of the patients in the placebo group experienced large reductions in TG even before being randomized. Use of the single baseline TG value at the time of randomization, in a post-hoc analysis, greatly attenuated and appears to explain much of this unusual placebo response. We look forward to the results of TRILOGY 2, which will further clarify the TG lowering effects of CaPre.”

The Company provided all of the TRILOGY 1 background information and accompanying data to the FDA in a Type C briefing package which was filed on April 29, 2020. The FDA provided Acasti with a written response to its Type C Meeting request and briefing package, and confirmed that it will require pivotal efficacy analyses for TRILOGY 2 to be performed on the full Intent to Treat (ITT) population, as contemplated in the original Statistical Analysis Plan (SAP), and they supported the conduct of post-hoc analyses in TRILOGY 1 for exploratory purposes. Consistent with the Company’s prior disclosures, and depending on the outcome of TRILOGY 2, an additional clinical study may still be needed prior to

submitting a New Drug Application (NDA). Acasti and its expert advisors are now carefully considering the FDA's comments on the TRILOGY 1 data and will conduct further post-hoc analysis based on their feedback.

Jan D'Alvise, president and CEO of Acasti, commented, "We made steady progress throughout fiscal 2020 by completing our TRILOGY Phase 3 trials in fiscal Q4, and advancing other important pre-commercialization activities, including scale-up of our manufacturing, NDA preparation, and certain partnering and market development objectives. While our initial topline results from TRILOGY 1 were disappointing due to the unusually large placebo effect, we now have a better understanding of the unusual "Pre-Randomization TG Normalization effect" that contributed significantly to the TRILOGY 1 outcome. We are carefully considering the FDA's comments on the TRILOGY 1 data, and are conducting further post-hoc analysis based on their feedback. Acasti will now finalize the Statistical Analysis Plan (SAP) for TRILOGY 2, which we plan to submit to the FDA by the end of July. We continue to remain blinded to the TRILOGY 2 data, and we continue to estimate that we should be able to report topline data by the end of August 2020. The key secondary and exploratory endpoints from both TRILOGY 1 and TRILOGY 2 trials would still be expected as soon as possible after the unblinding of TRILOGY 2 results."

D'Alvise continued, "In parallel with all of the TRILOGY activities in Fiscal 2020, we continued to make good progress on the preparation of our NDA package, and plans for commercial launch in the United States, assuming we are successful in gaining regulatory approval for CaPre. At the same time, we continued to strengthen our intellectual property portfolio. We are pleased to have been awarded additional composition of matter and method of use patents in Canada, United States, Mexico, China, Hong Kong, Chile, and Israel since the start of fiscal 2020. We believe all of these patents and pending patent applications increase potential commercial opportunities for CaPre, including through possible licensing and partnership opportunities. We are committed to building a global portfolio of patents to ensure long-lasting and comprehensive intellectual property protection, and to safeguard potentially valuable market expansion opportunities."

As of March 31, 2020, Acasti had cash, cash equivalents and short-term investments totaling $14.2 million, compared to $25.8 million as of March 31, 2019. The Company believes it is sufficiently funded into the first calendar quarter of 2021, based on management's current projections.

Other Developments:

- **On April 20, 2020**, Acasti announced receiving a Notice of Allowance for its second composition of matter patent to be awarded by the Canadian Intellectual Property Office. This new patent expands the Company's existing claims to include any composition containing EPA and DHA, where at least 50% of the composition consists of phospholipids.
- **On April 30, 2020**, Acasti reported receiving a notice of issuance of a composition of matter patent to be awarded by the Intellectual Property Office in Hong Kong granting claims for any composition containing EPA and DHA, where at least 50% of the composition consists of phospholipids.

Fiscal Year 2020 Financial Results (US dollars):

The consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP").

- **Loss from operations** for the year ended March 31, 2020 was $24.4 million, compared to a loss from operations of $34.4 million for the year ended March 31, 2019. The decrease was due mainly to a reduction in research contract expenses as the Phase 3 clinical program for CaPre was nearing completion.
- **Net loss** for the year ended March 31, 2020 was $25.5 million or $0.30 per share, compared to a net loss of $39.4 million or $0.73 per share for the year ended March 31, 2019. The decreased net loss is primarily due to the reduction of research and development expenses as the Phase 3 clinical program for CaPre was nearing completion, lower net financial expenses, and to the change in fair value of the warrant derivative liability.
- **R&D expenses** before depreciation, amortization and stock-based compensation expenses were $13.2 million for the year ended March 31, 2020, compared to $26.9 million for the year ended March 31, 2019. The $13.6 million decrease was mainly attributable to a $14.4 million decrease in research contracts, partially offset by an increase in salaries and benefits due to increased headcount and related benefits. The lower research contract expense is primarily attributed to the Phase 3 clinical trial program nearing completion.
- **General and Administrative expenses** before stock-based compensation expenses were $4.6 million for the year ended March 31, 2020, an increase of $1.3 million from $3.3 million for the year ended March 31, 2019. This increase was mainly attributable to a $0.45 million increase associated with the Company's insurance policies, as well as an increase of $0.83 million in corporate, accounting and legal fees associated with the implementation of a new ERP system, and the conversion of the financial reporting from IFRS to U.S. GAAP.
- **Sales and Marketing expenses** before stock-based compensation expenses were $2.4 million for the year ended March 31, 2020, compared to $0.42 million for the year ended March 31, 2019. The increase is in line with the planned increased headcount in the commercial team to support expanded business and market development activities.
- **Cash flows** – Cash and cash equivalents and short-term investments totaled $14.2 million as of March 31, 2020, compared to $25.8 million for the year ended March 31, 2019. As stated above, Acasti believes that existing cash will fully fund the Company's operations into the first calendar quarter of 2021. Acasti projects that additional funds will be needed in the future for activities necessary to prepare for the commercial launch of CaPre if regulatory approval is received, including the scale-up of its manufacturing operations, the completion of the potential regulatory NDA submission package (assuming positive Phase 3 clinical results), and the expansion of business development and U.S. commercial launch activities. The Company is working towards development of strategic partner relationships, as well as actively seeking additional non-dilutive funds in the near future, but there can be no assurance as to when or whether Acasti will complete any strategic collaborations or non-dilutive financings. If the Company does not raise additional funds or find one or more strategic partners, it may not be able to realize its assets and discharge its liabilities in the normal course of business. As a result, there exists substantial doubt about the Company's ability to continue as a going concern, and therefore, realize its assets and discharge its liabilities in the normal course of business.

Capital Markets Update:

Acasti provided an update on recent distributions under its previously adopted "at-the-market" equity offering program (the "ATM Program"), as required pursuant to the policies of the TSX Venture Exchange. Since the last distributions under the ATM program reported on February 14, 2020, Acasti issued an aggregate of 2,278,936 common shares (the "ATM Shares") over the NASDAQ Stock Market for aggregate gross proceeds to the Company of US$ 1.8 million. The ATM Shares were sold at prevailing market prices averaging US$ 0.81 per share. No securities were sold through the facilities of the TSX Venture Exchange or, to the knowledge of the Company, in Canada. The ATM Shares were sold pursuant to a U.S. registration statement on Form F-3 (No. 333-223464) as made effective on March 16, 2018, as well as an at-the-market issuance sales agreement dated February 14, 2019 among Acasti and B. Riley FBR, Inc. In addition, 81,925 common shares of the Company were issued over the NASDAQ Stock Market on December 13, 2019 for additional aggregate gross proceeds to the Company of US$167,946.25, which issuance was unintentionally omitted from the press release dated February 14, 2020 referenced above.

Conference Call

Acasti will host a conference call today, June 29, 2020 at 1:00 PM Eastern Time to discuss the Company's financial results for the year ended March 31, 2020, as well as provide an update on the TRILOGY Phase 3 program for CaPre.

The conference call will be available via telephone by dialing toll free 844-369-8770 for U.S. callers or +1 862-298-0840 for international callers, or on the Company's News and Investors section of the website: https://www.acastipharma.com/investors/.

A webcast replay will be available on the Company's News and Investors section of its website (https://www.acastipharma.com/investors/) through September 29, 2020. A telephone replay of the call will be available approximately one hour following the call, through July 6, 2020, and can be accessed by dialing 877-481-4010 for U.S. callers or +1 919-882-2331 for international callers and entering conference ID: 35330.

About CaPre (omega-3 phospholipid)

Acasti's prescription drug candidate, CaPre, is a highly purified omega-3 phospholipid concentrate derived from krill oil, and is being developed to treat severe hypertriglyceridemia, a metabolic condition that contributes to increased risk of cardiovascular disease and pancreatitis. Its omega-3s, principally EPA and DHA, are either "free" or bound to phospholipids, which allows for better absorption into the body. Acasti believes that EPA and DHA are more efficiently transported by phospholipids sourced from krill oil than the EPA and DHA contained in fish oil that are transported either by triglycerides (as in dietary supplements) or as ethyl esters in other prescription omega-3 drugs, which must then undergo additional digestion before they are ready for transport in the bloodstream. Clinically, the phospholipids may not only improve the absorption, distribution, and metabolism of omega-3s, but they may also decrease the synthesis of LDL cholesterol in the liver, impede or block cholesterol absorption, and stimulate lipid secretion from bile. In two Phase 2 studies, CaPre achieved a statistically significant reduction of triglycerides and non-HDL cholesterol levels in patients across the dyslipidemia spectrum from patients with mild to moderate hypertriglyceridemia (patients with TG blood levels between 200mg/dl and

500mg/dl) to patients with severe hypertriglyceridemia (those with TG levels above 500mg/dl). Furthermore, in the Phase 2 studies, CaPre demonstrated the potential to actually reduce LDL, or "bad cholesterol", as well as the potential to increase HDL, or "good cholesterol", especially at the therapeutic dose of 4 grams/day. The Phase 2 data also showed a significant reduction of HbA1c at a 4-gram dose, suggesting that due to its unique omega-3/phospholipid composition, CaPre may actually improve long-term glucose metabolism. Acasti's TRILOGY Phase 3 program is currently underway, as noted above.

About Acasti

Acasti is a biopharmaceutical innovator advancing a potentially best-in-class cardiovascular drug, CaPre, for the treatment of hypertriglyceridemia, a chronic condition affecting an estimated one third of the U.S. population. Since its founding in 2008, Acasti has focused on addressing a critical market need for an effective, safe and well-absorbing omega-3 therapeutic that can make a positive impact on the major blood lipids associated with cardiovascular disease risk. The Company is developing CaPre in a Phase 3 clinical program in patients with severe hypertriglyceridemia, a market that includes 3 to 4 million patients in the U.S. The potential exists to expand the treatable market in the United States to the approximately 50 million people with TGs above 150 mg/dl, given the recent FDA approval of expanded labeling for VASCEPA based on the recent positive REDUCE-IT outcome study results. Acasti may need to conduct at least one additional clinical trial to support FDA approval of a supplemental New Drug Application to expand CaPre's indications to this segment. Acasti's strategy is to commercialize CaPre in the U.S. and the Company is pursuing development and distribution partnerships to market CaPre in major countries around the world. For more information, visit www.acastipharma.com.

Forward Looking Statements

Statements in this press release that are not statements of historical or current fact constitute "forward-looking information" within the meaning of Canadian securities laws and "forward-looking statements" within the meaning of U.S. federal securities laws (collectively, "forward-looking statements"). Such forward-looking statements involve known and unknown risks, uncertainties, and other unknown factors that could cause the actual results of Acasti to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. In addition to statements which explicitly describe such risks and uncertainties, readers are urged to consider statements labeled with the terms "believes," "belief," "expects," "intends," "anticipates," "potential," "should," "may," "will," "plans," "continue", "targeted" or other similar expressions to be uncertain and forward-looking. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Forward-looking statements in this press release include, but are not limited to, information or statements about Acasti's strategy, future operations, prospects and the plans of management; Acasti's ability to conduct all required clinical and non-clinical trials for CaPre, including the timing and results of those trials; CaPre's potential to become the "best-in-class" cardiovascular drug for treating severe Hypertriglyceridemia; the timing and outcome of the unblinding of TRILOGY 2; and Acasti's ability to file an NDA based on the results of its TRILOGY Phase 3 program.

The forward-looking statements contained in this press release are expressly qualified in their entirety by this cautionary statement, the "Special Note Regarding Forward-Looking

Statements" section contained in Acasti's latest annual report on Form 10-K, which will be available on EDGAR at www.sec.gov/edgar/shtml, on SEDAR at www.sedar.com and on the investor section of Acasti's website at www.acastipharma.com. All forward-looking statements in this press release are made as of the date of this press release. Acasti does not undertake to update any such forward-looking statements whether as a result of new information, future events or otherwise, except as required by law. The forward-looking statements contained herein are also subject generally to assumptions and risks and uncertainties that are described from time to time in Acasti's public securities filings with the Securities and Exchange Commission and the Canadian securities commissions, including Acasti's latest annual report on Form 10-K under the caption "Risk Factors".

Neither NASDAQ, the TSX Venture Exchange nor its Regulation Services Provider (as that term is defined in the policies of the TSX Venture Exchange) accepts responsibility for the adequacy or accuracy of this release.

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