Caelum and Alexion Present Additional Phase 2 Data Reinforcing Safety and Tolerability of CAEL-101 in AL Amyloidosis at the European Hematology Association Congress 2021

June 11, 2021

- Exploratory biomarker analyses suggest possible cardiac disease improvements and renal response -

BORDENTOWN, N.J. & BOSTON--(BUSINESS WIRE)--Jun. 11, 2021-- Caelum Biosciences and Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced new Phase 2 safety and tolerability data for CAEL-101, a potentially first-in-class amyloid fibril targeted therapy, in combination with standard-of-care (SoC) therapy in patients with AL amyloidosis. The data, presented in two e-posters at the European Hematology Association (EHA) Congress 2021, strengthen the safety and tolerability profile of CAEL-101, further support the dose selection for the ongoing Phase 3 study, and suggest possible cardiac and renal response. An e-poster featuring the first data from a new arm of the study demonstrated that CAEL-101 administered in combination with cyclophosphamide-bortezomib-dexamethasone (CyBorD) plus daratumumab was generally safe and well-tolerated in the first four weeks of treatment. Data presented in a second e-poster showed longer-term evidence that CAEL-101 in combination with CyBorD was generally well-tolerated for a median treatment duration of 49 weeks, and exploratory clinical biomarker data suggesting possible cardiac disease improvements and renal response among patients with cardiac or renal impairment at baseline, respectively.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20210611005037/en/

“AL amyloidosis is a relentless disease that is particularly devastating when it impacts the heart, with some of these patients facing a median survival of less than one year following diagnosis. Current treatments for AL amyloidosis are designed to prevent or suppress the formation of new amyloids, but they do not address the existing amyloid buildup in the involved organs like the heart and kidneys, which can result in continued organ damage and can ultimately be fatal,” said Michael Spector, President and Chief Executive Officer of Caelum. “Understanding that CAEL-101 has the potential to be the first therapy to address the devastating organ damage caused by AL amyloidosis, we are urgently working to advance the ongoing CARES Phase 3 program in collaboration with Alexion.”

Safety and Tolerability of CAEL-101 in Combination with Cyclophosphamide-Bortezomib-Dexamethasone and Daratumumab in Patients with AL amyloidosis (#EP1017)

As was previously announced, the Phase 2 study of CAEL-101 in combination with CyBorD met its primary objectives, supporting the safety and tolerability of CAEL-101 and the selection of the 1000 mg/m^2 dose for the ongoing Phase 3 study. Results presented from an additional study arm that included 11 patients receiving CAEL-101 (1000 mg/m^2 dose) in combination with CyBorD plus daratumumab suggested that treatment with this combination was generally well-tolerated in the first four weeks of treatment. Specifically, adding daratumumab to the CAEL-101 and CyBorD regimen did not result in any new safety signals, nor did it alter the pharmacokinetic (PK) exposure to CAEL-101. The most common adverse events (AEs) reported in the first four weeks in the additional arm were nausea, constipation, and insomnia.

Safety and Tolerability of CAEL-101 in Patients with AL Amyloidosis in a Phase 2 Study for a Median of 49 Weeks (#EP1018)

Additional longer-term data presented from the Phase 2 study demonstrated that CAEL-101 in combination with CyBorD in patients with AL amyloidosis (N=13) was generally well tolerated up to a median treatment duration of 49 weeks (range 12-57 weeks), with most patients having received more than 20 infusions of CAEL-101. The most common AEs reported were diarrhea, nausea, fatigue, rash, and anemia. In addition, exploratory clinical biomarker evaluations showed early signals suggesting possible cardiac and renal response. Specifically, median percent changes for biomarkers of cardiac disease (cTnT and NT-proBNP) were lower at each subsequent time point measured, suggesting improvement in cardiac function among eight patients with active cardiac disease at baseline. Additionally, seven patients with active renal impairment at baseline demonstrated renal response, as defined by a decrease of at least 30 percent in proteinuria (an excess of protein in the urine) following treatment.

“We are grateful to clinical trial participants who are essential to advancing our work towards new treatment options for AL amyloidosis,” said John Orloff, M.D., Executive Vice President and Head of Research and Development at Alexion. “We remain committed to working together with the AL amyloidosis community and Caelum to evaluate the potential of CAEL-101 as a potentially first-in-class treatment option for patients who are living with this devastating disease.”

As was previously announced, the Cardiac Amyloid Reaching for Extended Survival (CARES) Phase 3 clinical program to evaluate CAEL-101 in combination with SoC therapy in AL amyloidosis has begun. Enrollment is underway in two parallel Phase 3 studies – one in patients with Mayo stage IIIa disease (ClinicalTrials.gov Identifier: NCT04512235) and one in patients with Mayo stage IIIb disease (ClinicalTrials.gov Identifier: NCT04504825) – and will collectively enroll approximately 370 patients globally.

About the CAEL-101 Phase 2 Study

The Phase 2 multicenter, open-label, dose-selection study (ClinicalTrials.gov Identifier: NCT04304144) is designed to evaluate the safety and tolerability of CAEL-101 in combination with standard of care (SoC) therapy for patients with AL amyloidosis and determine the recommended dose for Phase 3 studies. The study is divided into two parts: Part A examined CAEL-101 in combination with cyclophosphamide-bortezomib-dexamethasone (CyBorD) and employed a 3+3 dose escalation design (cohort 1 – 500 mg/m^2; cohort 2 – 750 mg/m^2 ; cohort 3 1000 mg/m^2); Part A patients were subsequently up titrated to 1000mg/m^2, once this was identified as the Phase 3 dose. Part B is examining CAEL-101 at the 1000 mg/m^2 dose in combination with CyBorD plus daratumumab. Patients from Parts A and B receive CAEL-101 therapy weekly for the four-week observation period followed by CAEL-101 doses every other week thereafter, all while continuing to receive SoC therapy. Patients continue to receive CAEL-101 per protocol until the end of the study or discontinuation.

About CAEL-101

CAEL-101 is a first-in-class monoclonal antibody (mAb) designed to improve organ function by reducing or eliminating amyloid deposits in the tissues and organs of patients with AL amyloidosis. The antibody is designed to bind to misfolded light chain proteins and amyloid and shows binding to both kappa and lambda subtypes. In a Phase 1a/1b study, CAEL-101 demonstrated improved organ function, including cardiac and renal function, in 27 patients with relapsed and refractory AL amyloidosis who had previously not had an organ response to standard of care therapy. CAEL-101 has received Orphan Drug Designation from both the U.S. Food and Drug Administration and European Medicine Agency as a potential therapy for patients with AL amyloidosis.

About AL Amyloidosis

AL amyloidosis is a rare systemic disorder caused by an abnormality of plasma cells in the bone marrow. Misfolded immunoglobulin light chains produced by plasma cells aggregate and form fibrils that deposit in tissues and organs. This deposition can cause widespread and progressive organ damage and high mortality rates, with death most frequently occurring as a result of cardiac failure. Current standard of care includes plasma cell directed chemotherapy and autologous stem cell transplant, but these therapies do not address the organ dysfunction caused by amyloid deposition, and up to 80 percent of patients are ineligible for transplant.

AL amyloidosis is a rare disease but is the most common form of systemic amyloidosis. There are approximately 22,000 patients across the United States, France, Germany, Italy, Spain and the United Kingdom. AL amyloidosis has a one-year mortality rate of 47 percent, 76 percent of which is caused by cardiac amyloidosis.

About Caelum Biosciences

Caelum Biosciences, Inc. (“Caelum”) is a clinical-stage biotechnology company developing treatments for rare and life-threatening diseases. Caelum’s lead asset, CAEL-101, is a novel antibody for the treatment of patients with amyloid light chain (“AL”) amyloidosis. In 2019, Caelum entered a collaboration agreement with Alexion under which Alexion acquired a minority equity interest in Caelum and an exclusive option to acquire the remaining equity in the company. Caelum was founded by Fortress Biotech, Inc. (NASDAQ: FBIO). For more information, visit www.caelumbio.com.

About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed and commercializes two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), as well as the first and only approved complement inhibitor to treat anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Alexion also has two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare metabolic disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D) as well as the first and only approved Factor Xa inhibitor reversal agent. In addition, the company is developing several mid-to-late-stage therapies, including a copper-binding agent for Wilson disease, an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases and an oral Factor D inhibitor as well as several early-stage therapies, including one for light chain (AL) amyloidosis, a second oral Factor D inhibitor and a third complement inhibitor. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on hematology, nephrology, neurology, metabolic disorders, cardiology, ophthalmology and acute care. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. This press release and further information about Alexion can be found at: www.alexion.com.

[ALXN-P]

Forward-Looking Statement

This press release contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Alexion (and Caelum) and their products, including statements related to: CAEL-101 is a potential first-in-class amyloid fibril targeted therapy; CAEL-101 clinical studies suggest possible positive cardiac and renal response; the anticipated or possible benefits of CAEL-101 for patients (including exploratory clinical biomarker data suggesting possible cardiac disease improvements and renal response among patients with cardiac or renal impairment at baseline); CAEL-101 has the potential to be the first therapy to address the devastating organ damage caused by AL amyloidosis; exploratory clinical biomarker evaluations showed early signals suggesting possible cardiac and renal response; Alexion remains committed to working together with the AL amyloidosis community and Caelum to evaluate the potential of CAEL-101 as a potentially first-in-class treatment option for patients who are living with this devastating disease; CAEL-101 is designed to improve organ function by reducing or eliminating amyloid deposits in the tissues and organs of patients with AL amyloidosis; CAEL-101 is designed to bind to misfolded light chain protein and amyloid and shows binding to both kappa and lambda subtypes; and characteristics of clinical trials for CAEL-101 including the number and type of patients expected to be enrolled in clinical trials. Forward-looking statements are subject to factors that may cause Alexion's or Caelum’s results and plans to differ materially from those expected by these forward looking statements, including for example: CAEL-101 may not generate the expected benefits to patients that are anticipated (including safety and efficacy benefits that were reported in earlier clinical trials); anticipated regulatory approvals may be delayed or declined; results of clinical trials may not be sufficient to satisfy regulatory authorities to approve CAEL-101 as a treatment for AL amyloidosis or other indication (or they may request additional trials or additional information); results in clinical trials may not be indicative of results from later stage or larger clinical trials (or in broader patient populations once the product is approved for use by regulatory agencies); the possibility that results of clinical trials are not predictive of safety and efficacy and potency of CAEL-101 (or failure to adequately operate or manage clinical trials) which could cause us or Caelum to discontinue sales of the product (or halt trials, delay or prevent submission of regulatory approval filings or result in denial of approval of product candidates); the severity of the impact of the COVID-19 pandemic on the businesses, including on commercial and clinical trial and clinical development programs; unexpected delays in clinical trials; unexpected concerns regarding product candidates that may arise from additional data or analysis obtained during clinical trials or obtained once used by patients following product approval; future product improvements may not be realized due to expense or feasibility or other factors; delays (expected or unexpected) in the time it takes regulatory agencies to review and make determinations on applications for the marketing approval of products; inability to timely submit (or failure to submit) future applications for regulatory approval for products and product candidates; inability to timely initiate (or failure to initiate) and complete future clinical trials due to safety issues, IRB decisions, CMC-related issues, expense or unfavorable results from earlier trials (among other reasons); Alexion dependence on sales from complement inhibitors; future competition from biosimilars and novel products; decisions of regulatory authorities

regarding the adequacy of the research, marketing approval or material limitations on the marketing of products; delays or the inability to launch product candidates due to regulatory restrictions, anticipated expense or other matters; interruptions or failures in the manufacture and supply of products and product candidates; failure to satisfactorily address matters raised by regulatory agencies regarding products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; the adequacy of pharmacovigilance and drug safety reporting processes; failure to protect and enforce our data, intellectual property and proprietary rights and the risks and uncertainties relating to intellectual property claims, lawsuits and challenges against us (including intellectual property lawsuits relating to ULTOMIRIS brought by third parties); the risk that third party payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all; failure to realize the benefits and potential of investments, collaborations, licenses and acquisitions; the possibility that expected tax benefits will not be realized; potential declines in sovereign credit ratings or sovereign defaults in countries where products are sold; delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement; adverse impacts on our supply chain, clinical trials, manufacturing operations, financial results, liquidity, hospitals, pharmacies and health care systems from natural disasters and global pandemics, including the coronavirus; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk that estimates regarding the number of patients with AL amyloidosis and other indications we are pursuing are inaccurate; the impact of the proposed transaction between Alexion and AstraZeneca plc; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructurings; and a variety of other risks set forth from time to time in Alexion's filings with the SEC, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 and in our other filings with the SEC. Alexion and Caelum disclaim any obligation to update any of these forward-looking statements to reflect events or circumstances after the date hereof, except when a duty arises under law.

Forward-Looking Statement Regarding Acquisition of Alexion by AstraZeneca

This communication contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are generally identified by the use of forward-looking terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “explore,” “evaluate,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” or “will,” or the negative thereof or other variations thereon or comparable terminology. These forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond Alexion’s and AstraZeneca plc’s “AstraZeneca”) control. Statements in this communication regarding Alexion, AstraZeneca and the combined company that are forward-looking, including anticipated benefits of the proposed transaction, the impact of the proposed transaction on Alexion’s and AstraZeneca’s businesses and future financial and operating results, the amount and timing of synergies from the proposed transaction, the terms and scope of the expected financing for the proposed transaction, the aggregate amount of indebtedness of the combined company following the closing of the proposed transaction, are based on management’s estimates, assumptions and projections, and are subject to significant uncertainties and other factors, many of which are beyond Alexion’s and AstraZeneca’s control. These factors include, among other things, market factors, competitive product development and approvals, pricing controls and pressures (including changes in rules and practices of managed care groups and institutional and governmental purchasers), economic conditions such as interest rate and currency exchange rate fluctuations, judicial decisions, claims and concerns that may arise regarding the safety and efficacy of in-line products and product candidates, changes to wholesaler inventory levels, variability in data provided by third parties, changes in, and interpretation of, governmental regulations and legislation affecting domestic or foreign operations, including tax obligations, changes to business or tax planning strategies, difficulties and delays in product development, manufacturing or sales including any potential future recalls, patent positions and the ultimate outcome of any litigation matter. Additional information concerning these risks, uncertainties and assumptions can be found in Alexion’s and AstraZeneca’s respective filings with the SEC, including the risk factors discussed in Alexion’s most recent Annual Report on Form 10-K, as updated by its Quarterly Reports on Form 10-Q, in AstraZeneca’s most recent Annual Report on Form 20-F and in each company’s future filings with the SEC. Important risk factors could cause actual future results and other future events to differ materially from those currently estimated by management, including, but not limited to, the risks that: a condition to the closing the proposed acquisition may not be satisfied; a regulatory approval that may be required for the proposed acquisition is delayed, is not obtained or is obtained subject to conditions that are not anticipated; AstraZeneca is unable to achieve the synergies and value creation contemplated by the proposed acquisition; AstraZeneca is unable to promptly and effectively integrate Alexion’s businesses; management’s time and attention is diverted on transaction related issues; disruption from the transaction makes it more difficult to maintain business, contractual and operational relationships; the credit ratings of the combined company declines following the proposed acquisition; legal proceedings are instituted against Alexion, AstraZeneca or the combined company; Alexion, AstraZeneca or the combined company is unable to retain key personnel; and the announcement or the consummation of the proposed acquisition has a negative effect on the market price of the capital stock of Alexion or AstraZeneca or on Alexion’s or AstraZeneca’s operating results. No assurances can be given that any of the events anticipated by the forward-looking statements will transpire or occur, or if any of them do occur, what impact they will have on the results of operations, financial condition or cash flows of Alexion or AstraZeneca. Should any risks and uncertainties develop into actual events, these developments could have a material adverse effect on the proposed transaction and/or Alexion or AstraZeneca, AstraZeneca’s ability to successfully complete the proposed transaction and/or realize the expected benefits from the proposed transaction. You are cautioned not to rely on Alexion’s and AstraZeneca’s forward-looking statements. These forward-looking statements are and will be based upon management’s then-current views and assumptions regarding future events and operating performance, and are applicable only as of the dates of such statements. Neither Alexion nor AstraZeneca assumes any duty to update or revise forward-looking statements, whether as a result of new information, future events or otherwise, as of any future date.

View source version on businesswire.com: https://www.businesswire.com/news/home/20210611005037/en/

Caelum Contacts:
Company
Michael Spector, President & Chief Executive Officer
mspector@caelumbio.com

Jaclyn Jaffe and Bill Begien
Investor Relations
(781) 652-4500
info@caelumbio.com

Media

Tony Plohoros
6 Degrees
(908) 591-2839
tplohoros@6degreespr.com

Alexion Contacts:
Media
Lisa Taylor, 857-338-9025
Senior Director, Corporate Communications

Investors
Chris Stevo, 857-338-9309
Head of Investor Relations

Source: Alexion Pharmaceuticals, Inc.