Achillion Reports Positive Data from Phase 2 Study of Danicopan (ACH-4471) in Combination with Eculizumab in PNH Patients who Have an Inadequate Response to Eculizumab Monotherapy at the 61st American Society of Hematology Meeting

December 9, 2019

– 2.4 g/dL mean increase in hemoglobin at 24 weeks –
– Reduction in blood transfusions from 34 to 1; and improvements in markers of hemolysis –
- Completed End of Phase 2 Meeting; Phase 3 Trial Initiation in early 2020 -

BLUE BELL, Pa., Dec. 09, 2019 (GLOBE NEWSWIRE) -- Achillion Pharmaceuticals, Inc. (Nasdaq: ACHN), a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients and families affected by complement-mediated diseases, today reported top-line data from a dose-finding Phase 2 trial assessing the safety and effectiveness of its oral small molecule factor D inhibitor danicopan (ACH-4471) in combination with intravenous eculizumab in paroxysmal nocturnal hemoglobinuria (PNH) patients who have an inadequate response to C5 monotherapy. Data from the Phase 2 trial were presented in a poster presentation today at the 61st American Society of Hematology (ASH) Annual Meeting in Orlando, FL.

The primary endpoint of the trial was an increase in hemoglobin from baseline. A mean increase of 2.4 g/dL at 24 weeks of treatment was achieved in this proof-of-concept trial. Danicopan, in combination with eculizumab, resulted in a significant reduction in blood transfusions with 10 patients receiving 34 transfusions (58 units) in the 6 months prior to screening to 1 patient receiving 1 transfusion (2 units) during the 24-week trial.

Phase 2 Open-label Study of Danicopan in Patients with PNH who Have an Inadequate Response to Eculizumab Monotherapy

	Baseline N=11 Mean	**Week 24 N=11 Mean**
Lab Parameters		
Hgb (g/dL)	7.9	10.3
LDH (xULN)	1.06	1.04
Reticulocytes (xULN)	2.3	1.4
Total bilirubin (xULN)	2.17	1.35
Direct bilirubin (xULN)	1.6	1.2
PNH red cell clone size (%)	54	84*
C3 fragment deposition on PNH RBCs (%)	30	18
Transfusions N = 10**	24 Weeks Prior	24 Week Trial
Number of transfusions	34	1
Units of blood	58	2
Quality of Life		
FACIT-Fatigue (Max Score 52)***	34	45

* **N**=7; for four patients, samples were out of stability range.

** N=10; Patient A excluded from transfusion results due to religious objection to receiving transfusions; baseline Hgb = 5 g/dL.

***Scores based on the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT) Fatigue Scale V4. Score range 0-52. A score of less than 30 indicates severe fatigue.

“C5 inhibition, the current standard of care, is an effective treatment approach for patients with PNH. While this treatment approach shows control of intravascular hemolysis and improved overall survival, many patients remain anemic and some may continue to be transfusion dependent due to persistent extravascular hemolysis,” stated Dr. Austin Kulaskeraraj MBBS, MD, MRCP, FRCPath, lead author of this Phase 2 poster presentation at ASH and consultant hematologist at Kings College Hospital in London. “In this clinical trial, the addition of danicopan, a factor D inhibitor that addresses the extravascular hemolysis caused by PNH, to C5 inhibitor therapy resulted in a greater than 2-gram increase in hemoglobin, and significant reduction of transfusions.”

In addition to improvements in hemoglobin and transfusions, there were also meaningful improvements in markers of hemolysis including bilirubin, reticulocytes, and PNH red blood clone size (%). “The increase in PNH specific red blood cell clone size, and reduction of reticulocytes, is likely due to the prevention of C3-mediated extravascular hemolysis, a result of targeting upstream in the Alternative Pathway, while retaining the control of MAC-mediated intravascular hemolysis,” said Dr. Steven Zelenkofske, Chief Medical Officer of Achillion. “The mean increase of 11 points on the FACIT Fatigue scale, relative to the baseline on eculizumab monotherapy, demonstrates the potential impact the addition of danicopan can have on a patient’s quality of life.”

In this clinical trial, danicopan was generally well tolerated. All treatment emergent adverse events were considered mild to moderate in severity except for Grade 3 severe adverse events that occurred in two patients. Both patients had resolution of their events, remained on danicopan, and completed the study.

The Company was granted Breakthrough Therapy designation by Food & Drug Administration (FDA) in September and PRIME designation by the European Medicines Agency (EMA) in November for danicopan for the treatment of PNH in combination with a C5 monoclonal antibody for patients who are suboptimal responders to a C5 inhibitor therapy alone. In addition, the Company met with the FDA during an End of Phase 2 Meeting in the

fourth quarter and is progressing to Phase 3. The Company plans to initiate a global Phase 3 trial in early 2020.

The poster presentation detailing the Phase 2 top-line results is being presented today, December 9, at approximately 10 a.m. EST at 61st American Society of Hematology (ASH) Annual Meeting and will be available on the Company's website at http://achillion.com/scientific-presentations.

Presentation Details
Poster Presentation: "A Phase 2 Open-Label Study of Danicopan (ACH-0144471) in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Who Have an Inadequate Response to Eculizumab Monotherapy"
Abstract Number: 3514
Session Name: 101. Red Cells and Erythropoiesis, Structure and Function, Metabolism, and Survival, Excluding Iron: Poster III
Session Date: Monday, December 9, 2019
Presentation Time: 6:00 PM – 8:00 PM
Location: Hall B

Danicopan (ACH-4471) Phase 2 Add-on Trial with Eculizumab

Danicopan was evaluated as an add-on with eculizumab, an intravenous C5 inhibitor that is currently approved as monotherapy for PNH. This is a Phase 2, open-label, multiple dose trial in adult patients on stable eculizumab treatment with blood transfusion dependent anemia, defined as receiving at least one transfusion in the 12 weeks prior to the study and a hemoglobin level below 10 g/dL. In addition to their usual dose of eculizumab, patients were administered danicopan orally three times a day at a dose determined by patient clinical response. The primary outcome of the trial is the change in hemoglobin at 24 weeks compared to baseline. Secondary outcomes include the number of blood transfusions required, impact on selected clinical parameters, and safety. Patients completing the study were eligible to enroll in a long-term extension study continuing on danicopan and their C5 background therapy of eculizumab or ravulizumab.

About Paroxysmal Nocturnal Hemoglobinuria

PNH is a rare, acquired blood disease caused by a somatic mutation resulting in the absence of key receptors, CD55 and CD59, on the surface of red blood cells (RBCs). The complement system recognizes these unprotected RBCs as foreign and destroys them in the circulatory system (intravascular hemolysis [IVH]) and in the liver or spleen (extravascular hemolysis [EVH]). The current standard of care for PNH targets IVH by inhibiting C5 complement protein (C5), leaving some patients with persistent EVH from early phases of complement activation (alternative pathway [AP] activity) which C5 inhibition cannot address. This may leave patients with partial control of their PNH symptoms. Up to seventy-five percent of PNH patients treated with C5 inhibitors remain anemic during treatment, with up to one-third of those patients reporting the need for blood transfusions within the last year. Factor D is the critical, rate-limiting protein within the AP. By targeting Factor D, proximal AP inhibition may disable both downstream terminal complement activation (IVH) and upstream C3 fragment opsonization (EVH). Achillion is developing a potentially more complete approach to PNH with factor D inhibition to selectively block alternative pathway activity and protect against both destructive processes of RBCs in PNH with convenient oral therapies.

More information is available at http://www.achillion.com/patients-and-clinicians/.

About the Achillion Complement Factor D Portfolio
Achillion has leveraged its internal discovery capabilities and a novel complement-related platform to develop oral small molecule drug candidates that are inhibitors of complement factor D. Factor D is an essential serine protease involved in the AP of the complement system, a part of the innate immune system. Achillion's complement platform is focused on seeking to advance oral small molecules that inhibit the AP and can potentially be used in the treatment of immune-related diseases in which complement AP plays a critical role. Potential indications currently being evaluated for these compounds include PNH, C3 glomerulopathy (C3G), and immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN).

About Achillion Pharmaceuticals
Achillion Pharmaceuticals, Inc. (Nasdaq: ACHN) is a clinical-stage biopharmaceutical company focused on advancing its oral small molecule complement inhibitors into late-stage development and commercialization. Research has shown that an overactive complement system plays a critical role in multiple disease conditions including the therapeutic areas of nephrology, hematology, ophthalmology and neurology. Achillion is initially focusing its drug development activities on complement-mediated diseases where there are no approved therapies or where existing therapies are inadequate for patients. Potential indications being evaluated for its compounds include paroxysmal nocturnal hemoglobinuria (PNH), C3 glomerulopathy (C3G), and immune complex membranoproliferative glomerulonephritis (IC-MPGN). Each of the product candidates in the Company's oral small molecule portfolio was discovered in its laboratories and is wholly owned. To achieve its goal of advancing its investigational product candidates into Phase 3 clinical trials and commercialization, the Company plans to work closely with key stakeholders including healthcare professionals, patients, regulators and payors.

More information is available at http://www.achillion.com.

Cautionary Note Regarding Forward-Looking Statements
This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other important factors that could cause actual results to differ materially from those indicated by such forward-looking statements. Achillion may use words such as "expect," "anticipate," "project," "target," "intend," "plan," "aim," "believe," "seek," "estimate," "can," "could," "focus," "will," "look forward," "continue," "goal," "strategy," "objective," "may," "potential," and similar expressions to identify such forward-looking statements. These forward-looking statements include statements about: the potential benefits of FDA's Breakthrough Designation and EMA's PRIME designation for danicopan; the potential benefits of factor D inhibition as a treatment for complement-mediated diseases, including danicopan (ACH-4471) for PNH; Achillion's expectations regarding the advancement of, and timeline for reporting results from, clinical trials of its product candidates (including danicopan and ACH-5228); Achillion's expectations regarding the timing of regulatory interactions and filings; and other statements concerning Achillion's strategic goals, efforts, plans, and prospects. Among the important factors that could cause actual results to differ materially from those indicated by such forward-looking statements are risks relating to, among other things, Achillion's ability to: continue to meet the clinical development program criteria for Breakthrough Designation and PRIME designation; accelerate the development timeline for danicopan utilizing benefits available through the Breakthrough Designation and PRIME designation; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its product candidates, including danicopan and ACH-5228; advance the preclinical and clinical development of its complement factor D inhibitors under the timelines it projects in current and future preclinical studies and clinical trials; whether

interim results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials or preclinical studies will be indicative of the results of later clinical trials; enroll patients in its clinical trials on its projected timelines; obtain and maintain patent protection for its product candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals, and the granting of orphan designation does not alter the standard regulatory requirements and process for obtaining such approval; establish commercial manufacturing arrangements; identify, enter into and maintain collaboration and other commercial agreements with third-parties; compete successfully in the markets in which it seeks to develop and commercialize its product candidates and future products; manage expenses; manage litigation; raise the substantial additional capital needed to achieve its business objectives; and successfully execute on its business strategies. These and other risks are described in the reports filed by Achillion with the U.S. Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2019, and any other SEC filings that Achillion makes from time to time.

In addition, any forward-looking statement in this press release represents Achillion's views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Achillion disclaims any duty to update any forward-looking statement, except as required by applicable law.

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