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Achillion Reports Preliminary Proof-of-Concept With ACH-4471 for the Treatment of C3G

- Greater than 50% improvement in proteinuria (albumin to creatinine ratio) after 14 days of oral dosing with ACH-4471 -

- Improvement in complement alternative pathway biomarkers observed -

NEW HAVEN, Conn., Nov. 14, 2017 (GLOBE NEWSWIRE) -- **Achillion Pharmaceuticals, Inc.** (Nasdaq:ACHN) today reported preliminary proof-of-concept results from group 1 of its ongoing Phase 2, open-label, 14-day study of ACH-4471 for patients with C3 glomerulopathy (C3G) or immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN). The Principal Investigator for this study is Dr. Tom Barbour, Royal Melbourne Hospital, Melbourne, Australia, Department of Nephrology.

This trial, initiated in September 2017, has currently completed treatment of the first group consisting of two sentinel patients. Interim data from the two sentinel patients in this ongoing trial demonstrated that ACH-4471 achieved complement alternative pathway (AP) inhibition resulting in a greater than 50% reduction in proteinuria, as measured by albumin to creatinine ratio (ACR), over the 14-day treatment period, and demonstrated a favorable tolerability profile.

"Preliminary data from this Phase 2 trial suggest that ACH-4471 may reverse the AP hyperactivity in C3G based upon the observed improvements in fragment: intact C3 and proteinuria with 14 days of treatment with ACH-4471," commented Milind Deshpande, Ph.D., President and Chief Executive Officer of Achillion. "We are excited by these early data and the potential of ACH-4471 to be a novel and potentially disease-modifying treatment for C3G and IC-MPGN."

The on-going Phase 2 trial is assessing whether ACH-4471 can reverse AP hyperactivity which is believed to be the underlying driver of the pathogenesis and progression of C3G. Patients with biopsy-established C3G or IC-MPGN with evidence of AP hyperactivity are eligible for enrollment. Multiple complement biomarkers indicative of AP activity, including the ratio of C3 fragments to intact C3 in plasma (fragment: intact C3), plasma Bb levels, ex vivo Ba formation, and Ba levels in urine were measured. Additional measures being evaluated include proteinuria, safety, and pharmacokinetics. Preliminary data from this Phase 2 trial suggest that ACH-4471 may have the potential to reverse AP hyperactivity resulting in improvement in proteinuria.

Per protocol, group 1 evaluated the safety and activity of 100 mg of ACH-4471 administered three times daily (TID) for 14 days, followed by a seven-day taper period, and a subsequent follow-up period. Achillion is currently screening patients for group 2 and plans to enroll up to eight C3G or IC-MPGN patients to evaluate additional doses of ACH-4471. Interim results from the two patients enrolled in group 1 are summarized below.

In C3G, the underlying pathophysiology is believed to be an overactive AP, mediated by increased C3 convertase activity. This increase in AP C3 convertase activity leads to excessive consumption of intact C3, and consequent elevations in the levels of C3 breakdown products, or C3 fragments. The subsequent deposition of these C3 fragments into the kidney is thought to be responsible for kidney damage and loss of function seen in this disease over time. As an inhibitor of factor D, ACH-4471 may be able to normalize AP activity in these patients, decreasing the excessive breakdown of intact C3. This change may be assessed by evaluating the ratio of C3 fragments to intact C3.

Both Patient A and Patient B are adult male patients diagnosed with C3G based upon historical kidney biopsy. Patient A had a baseline Bb, a byproduct of the interaction between factor D and factor B, at the upper limit of normal and achieved a 30% reduction in Bb levels, consistent with reductions observed in previously conducted Phase 1 healthy volunteer studies. Patient B had a significantly elevated Bb level at baseline and experienced near normalization with approximately a 50% reduction in Bb, during the treatment period with ACH-4471.

At baseline, Patient A had an elevated fragment: intact C3 ratio that was approximately 178% of the upper limit of normal (ULN) at baseline, which rapidly improved with normalization during the dosing period. Similarly, Patient B had an elevated fragment: intact C3 ratio that was approximately 187% of the ULN at baseline with a rapid decrease after initiation of dosing with an improvement to approximately 134% of the ULN by day 14. As an additional assessment of AP activity and inhibition after dosing with ACH-4471, an ex vivo assay was conducted in which Ba production was measured as a means of quantitating the ability to generate newly formed AP C3 convertase. Ba production serves as a proxy for newly formed AP C3 convertase since factor B can only be cleaved by factor D when it is already complexed with the components required to form the active AP C3 convertase. In this assay a 90%, or greater, reduction in the ability to form new AP convertase was observed for both Patients A and B throughout the dosing period.

In both Patients A and B, the primary clinical manifestation was significant proteinuria (baseline ACR > 200 mg/mmol). In both cases, a greater than 50% reduction in proteinuria, as measured by ACRs, was observed during the treatment period.

Subject		Albumin:Creatinine Ratio (ACR)	C3 fragment/intact	Ex vivo Ba production %
	Normal range	0 - 2.5 mg/mmol	0.0085 - 0.0949 (ratio)	NHS 100%
Patient A	Baseline	259.3	0.1692	132%
	On treatment	114.5 (day 17)	0.0606 (day 14)	35% (day 15)
	% Reduction	56%	64%	97%
Patient B	Baseline	580.3	0.1775	142%
	On treatment	263 (day 17)	0.1273 (day 14)	40% (day 14)
	% Reduction	55%	28%	102%

"C3G is a serious renal disease for which there are no FDA-approved therapies," commented Dr. Matthew Pickering, Professor of Rheumatology, Imperial College of London, who focuses on studying the role of complement and the mechanisms of kidney injury in C3G. "I am pleased to see these early data in which the biologic effects on complement proteins following administration with ACH-4471 indicated that this may represent a novel and promising approach for the treatment of C3G. Importantly, I am particularly encouraged by the magnitude of change in proteinuria this early in the treatment period. I look forward to results from additional patients and the potential for longer-term treatment durations with ACH-4471." Dr. Pickering is a paid scientific advisor for Achillion and Lead Investigator for an Achillion-sponsored Natural History Study in C3G.

(Clinicaltrials.gov: NCT03124368 /EudraCT: 2016-003525-42)

C3G / IC-MPGN: Phase 2 12-month open-label trial of ACH-4471

Achillion also plans to conduct a Phase 2 open-label, 12-month treatment trial for patients with biopsy-confirmed C3G or IC-MPGN. All patients enrolled will receive treatment with ACH-4471 with periodic assessment of clinical endpoints including proteinuria and estimated glomerular filtration rate (eGFR). Up to 20 patients are expected to be enrolled. Enrollment is expected to be initiated in the first half of 2018.

C3G: Phase 2 6-month randomized, placebo-controlled trial of ACH-4471

During the first half of 2018, Achillion plans to initiate a randomized, placebo-controlled, double-blinded Phase 2 trial evaluating the efficacy and safety of ACH-4471 in patients with C3G. The trial is designed to assess renal biopsy findings and clinical endpoints such as proteinuria and eGFR. Up to 20 patients are expected to be enrolled.

C3G / IC-MPGN: Global Natural History Study

Achillion is supporting a global natural history study of C3G and IC-MPGN, to track the course of this disease over time. The study is being led by Dr. Matthew Pickering and Dr. H. Terry Cook, both of Imperial College of London, in collaboration with C3G nephrologists worldwide. The aim of this study is to collect data on disease progression. This study, which began earlier this year, will run in parallel with other C3G clinical trials, and the data from this study are expected to inform and support product development and potential approval.

Achillion has solicited and received scientific advice from the FDA, the European Medicines Agency and the Medicines and Healthcare Products Regulatory Agency with respect to the design of the Phase 2 trials for C3G and paroxysmal nocturnal hemoglobinuria (PNH) and the safety monitoring plan, as well as, the plans for clinical pharmacology and nonclinical studies needed to support potential future registration for ACH-4471. In addition, investigational new drug applications are open in the United States for both PNH and C3G.

About the Achillion Complement Factor D Platform

Achillion has leveraged its internal discovery capabilities and a novel complement-related platform to develop small molecule drug candidates that are oral inhibitors of complement factor D. Factor D is an essential serine protease involved in the complement pathway, a part of the innate immune system. Achillion's complement platform is focused on seeking to

advance small molecule compounds that inhibit factor D and can potentially be used in the treatment of immune-related diseases in which complement alternative pathway plays a critical role. Potential indications being evaluated for these compounds include paroxysmal nocturnal hemoglobinuria (PNH), C3 glomerulopathy (C3G), immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN), and geographic atrophy (GA).

About Achillion Pharmaceuticals

Achillion Pharmaceuticals, Inc. (NASDAQ:ACHN) is a science-driven, patient-focused company seeking to leverage its strengths across the continuum from discovery to commercialization in its goal of providing better treatments for people with serious diseases. The company employs a highly-disciplined discovery and development approach that has allowed it to pursue best-in-class oral antiviral therapy for chronic hepatitis C (HCV) and build a platform of potent and specific complement inhibitors. Achillion is rapidly advancing its efforts to become a fully-integrated pharmaceutical company with a goal of bringing life-saving medicines to patients with rare diseases. 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," "goal," and "may" and similar expressions to identify such forward-looking statements. These forward-looking statements also include statements about: Achillion's expected plans, timing, data readouts and results from ongoing and planned clinical trials and natural history studies of ACH-4471; the potential therapeutic effects and benefits of ACH-4471 as a treatment for C3G, IC-MPGN and other indications; and statements concerning Achillion's strategic goals, milestone 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: advance the preclinical and clinical development of ACH-4471 under the timelines it projects in current and future preclinical studies and clinical trials; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; replicate in later cohorts or later trials any favorable results from earlier cohorts and earlier trials; obtain and maintain necessary regulatory approvals; establish commercial manufacturing arrangements; identify, enter into and maintain collaboration 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 Annual Report on Form 10-K for the year ended December 31, 2016, its Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2017, and its other SEC filings.

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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