

ACH-2684 is a potent pan-genotypic inhibitor of HCV protease. Preclinical studies demonstrate its excellent potency in the low pico-molar range, safety and tolerability, and a pharmacokinetic profile supportive of once daily dosing with excellent metabolic stability. The potency and virology profile of ACH-2684 demonstrates that it very effectively suppresses a broad range of natural variants of the hepatitis C virus, and may be effective in prevention and treatment of emerging resistant variants.

ACH-2684 AT-A-GLANCE

- **Potency.** With potency in the low pico-molar range, ACH-2684 is ten to twenty fold more potent than other HCV inhibitors under development.
- **Virology.** ACH-2684 demonstrates very effective suppression against a broad range of natural variants of the hepatitis C virus, and may be effective in prevention and treatment of emerging resistant variants and retains potent activity against all genotypes 1 through 6.
- **Combination Use.** It has been demonstrated *in vitro* that ACH-2684 can be used in combination with other HCV inhibitors and it is synergistic with NS5B nucleoside polymerase inhibitors.

Goals for New HCV Therapeutic Development

- Improving efficacy against the genotype 1 virus
- Offering a treatment response in patients who have failed an interferon and ribavirin-based treatment
- Reducing treatment-related adverse effects
- Offering a more convenient, orally available, treatment option

HCV Market Opportunity

It is estimated that over 170 million people are infected with HCV worldwide. The American Association of Liver Disease estimates that up to 85% of individuals become chronically infected following exposure to the virus. The current standard of care (SOC) for patients with chronic HCV infection is treatment with a combination of long-acting, pegylated forms of interferon alpha (IFN-alpha) administered through weekly injections coupled with twice daily, oral doses of ribavirin. The duration of treatment for HCV patients infected with the genotype 1 virus is 12 months and is successful in only approximately 50% of patients receiving a full course of treatment. Up to 40% of those patients modify or discontinue therapy due to adverse side effects, including flu-like symptoms, anemia, depression, fatigue, suicidal tendencies and abnormal fetal development.

Protease Inhibitor Program Overview

Our proprietary HCV protease inhibitors were designed and synthesized based on crystal structures of enzyme/inhibitor complex. Comprehensive *in vitro* and *in vivo* profiling was utilized for progression of potent inhibitors. The very high potency of ACH-2684 was achieved by designing the compound to optimize the way in which it binds with the NS3 protease. *In vitro* demonstrates that it effectively suppresses a broad range of natural variants of the hepatitis C virus, may be effective in the prevention and treatment of emerging resistant variants, and most importantly retains potent activity against all genotypes.

Preclinical and Clinical Development

In preclinical testing, ACH-2684 demonstrated activity *in vitro* against all genotypes of HCV at very low concentrations of less than 100 pico-molar. ACH-2684 demonstrated high safety margins in animals with minimal dose-related side effects in both single ascending-dose and multiple dose trials. The compound is metabolically stable and is rapidly and extensively partitioned in the liver, therefore supporting once-daily dosing in clinical development. An IND application for ACH-2684 was filed and a clinical program has commenced evaluating ACH-2684 in a first-in-man Phase 1 trial.

ACH-2684: Relative *In vitro* Potency

ID	Fold Increase in Potency over Telaprevir		
	EC ₅₀	EC ₉₀	EC ₉₅
ACH-2684	1567	2875	4174
TMC-435	188	310	264
MK-7009	256	206	216
telaprevir	1	1	1

ABOUT ACHILLION Achillion is an innovative biopharmaceutical company dedicated to bringing important new treatments to patients with infectious disease. The Company's highly skilled and experienced discovery and development teams have identified multiple small molecules with novel mechanisms of action, and is currently advancing three compounds for HCV infection through development. Achillion is focused on solutions for the most challenging problems in hepatitis and resistant bacterial infections.

Achillion Pharmaceuticals, Inc.
 300 George Street
 New Haven, CT 06511
 Main phone: 203.624.7000
 Email: info@achillion.com
 www.achillion.com