

The NS5A protein is a clinically validated mechanism of action whereby it serves multiple functions at various stages of the viral life cycle including involvement in virion production, interacting with host proteins and is implicated in interferon-resistance. In early preclinical studies, **ACH-2928** demonstrated excellent potency against HCV RNA replication, as well as good pharmacokinetic and safety profiles.

ACH-2928 AT-A-GLANCE

- **Potency.** Has demonstrated excellent potency against HCV RNA replication in all genotypes at concentrations ranging from 2 – 20pM.
- **Combinability.** ACH-2928 is highly effective in combination with NS3 protease inhibitors, NS5B polymerase inhibitors, interferon and ribavirin. *In vitro* it has additive to synergistic effects with Achillion's protease inhibitors.
- **Pharmacokinetics.** ACH-2928 is anticipated to be dosed once-daily without boosting.
- **Safety.** Has demonstrated a good safety profile at high doses.

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 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.

Preclinical Data and Clinical Development

Preclinical Data ACH-2928 has very high potency in the picomolar range, and is highly active across a broad range of HCV genotypes, including genotype 1a and 1b variants. ACH-2928 exhibits a good safety and pharmacokinetic profile that strongly suggests once-daily dosing, and is highly effective in combination with NS3 protease inhibitors, NS5B polymerase inhibitors, interferon and ribavirin.

ACH-2928: Activity Against Genotype 1a Replicon

| Inhibitor | H77 Replicon | Patient ID 1003 | Patient ID 800 | Patient ID 8005 | Patient ID 9002 |
|-----------------|--------------|-----------------------|----------------|-----------------|-----------------|
| | | EC ₅₀ (pM) | | | |
| ACH-2928 | 20 | 17 | 10 | 15 | 9 |

ACH-2928: Activity Against Genotype 1b Replicon

| Inhibitor | Huh-luc/neo (Readout: Luciferase) | | Huh-9-13 (Readout: HCV RNA) | |
|-----------------|-----------------------------------|-----------------------|-----------------------------|-----------------------|
| | EC ₅₀ (pM) | EC ₉₀ (pM) | EC ₅₀ (pM) | EC ₉₀ (pM) |
| ACH-2928 | 2 | 7.4 | 2.6 | 7.9 |

An IND application for ACH-2928 was filed and a clinical program is commencing evaluating ACH-2928 in a first-in-man Phase 1 trial.

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.

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