



One of Achillion's HCV approaches focused on the discovery of product candidates specific to a novel target, the HCV non-structural protein 4A or NS4A, a key component in viral replication. Through its in-house discovery efforts and as part of its collaboration with Gilead Sciences, Achillion has assembled a portfolio of next-generation antagonists to NS4A that are potent inhibitors of HCV replication. The most advanced of these compounds is ACH-1095.

### 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 magnitude of treatment-related adverse side effects, and
- Offering a more convenient, orally available, treatment option.

### ACH-1095 ADVANTAGES

- **Novel Mechanism of Action.** Achillion believes the unique mechanism of ACH-1095 may contribute to the lack of cross resistance between its compounds and other HCV inhibitors.
- **Potency.** Data obtained in standard laboratory assays demonstrate that ACH-1095 has potency *in vitro* 14 to 21 times greater than certain other protease inhibitors under clinical development.
- **Lack of Cross Resistance.** In laboratory studies, ACH-1095 has not demonstrated cross resistance to any of the polymerase inhibitors or protease inhibitors of which the Company is aware and has tested.
- **Potential for Combination Treatment.** Because of the synergy in *in vitro* tests with other classes of HCV inhibitors, Achillion believes that NS4A antagonists are well positioned as a treatment for chronic HCV in combination with the current standard of care and/or in combination with other direct-acting antivirals.

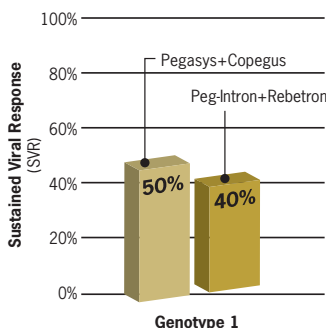
### Collaboration with Gilead Sciences, Inc.

In 2004, Achillion entered into a research collaboration and license agreement with Gilead Sciences, Inc. for the development and commercialization of compounds for the treatment of chronic hepatitis which inhibit HCV replication through a novel mechanism of action targeting the NS4A protein. Achillion could receive up to \$157.5 million in development, regulatory and sales milestone payments, assuming the successful simultaneous development of a lead and back-up compound, as well as royalties on net sales of products. In 2009, Achillion and Gilead modified their collaboration to allow Achillion to advance ACH-1095 independently, subject to an opt-in right by Gilead.

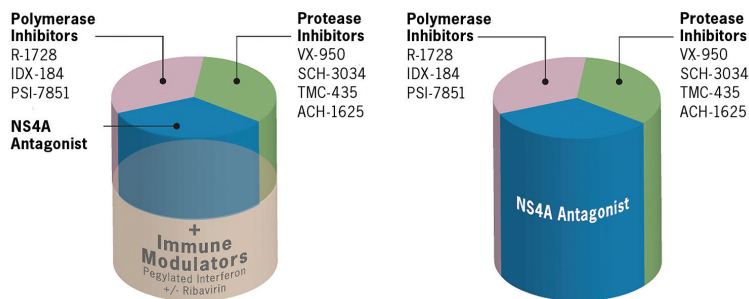
### HCV Market Opportunity

It is estimated that over 170 million people are infected with HCV worldwide and 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 daily, oral doses of ribavirin. The duration of treatment for 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.

As a result of their novel mechanism of action, broad potency against HCV, potential for oral administration and demonstrated lack of cross resistance, Achillion believes there could be significant commercial opportunity for its series of compounds targeting NS4A.



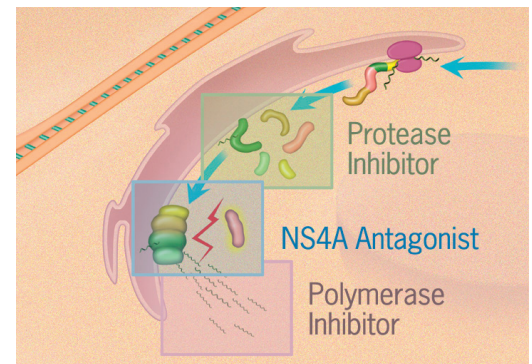
The current standard of care for HCV has significant limitations with less than half of patients receiving a full course of treatment.



As the HCV market evolves towards a combination therapy paradigm, Achillion's NS4A inhibitors are ideally positioned commercially as the only inhibitors that are under development in this novel target class, whether or not immunomodulatory therapy remains an element of the combination.

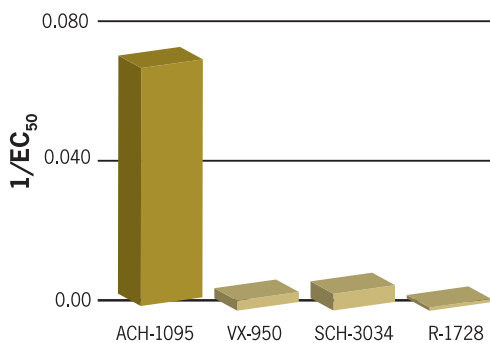
## Novel Mechanism of Action

Based upon extensive virology and biochemistry studies, the mechanism of action of these compounds appears to be novel and involves targeting the NS4A protein of HCV. Inhibiting this target prevents the formation of a functional replicase complex, a necessary step in viral replication that occurs before copying the viral RNA genome. Achillion believes this unique mechanism may contribute to the lack of cross resistance between its compounds and other HCV inhibitors.

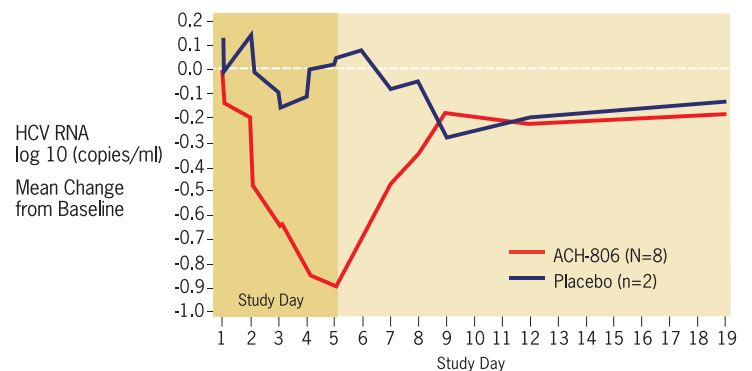


## Data Overview

**Preclinical Development** In preclinical studies, Achillion has demonstrated that NS4A antagonists inhibit HCV replication in cell-based replicon assays that have developed resistance to HCV protease and polymerase inhibitors. A series of similar compounds have demonstrated potent activity, as well as acceptable pharmacokinetic and safety profiles.



Achillion has compared the potency of its NS4A antagonists, including ACH-1095, with NS3 protease inhibitors currently in development, VX-950 developed by Vertex, and SCH-3034 developed by Schering-Plough, and found its NS4A antagonists to be more potent.



At the April 2007 meeting of the European Association for the Study of Liver Disease (EASL), Achillion presented data on its first NS4A antagonist, ACH-806, in a Phase 1 study in HCV genotype 1-infected individuals. This study provided the first demonstration of human antiviral activity of an NS4A antagonist for HCV.

**Clinical Development** Until February 2007, Achillion was pursuing clinical development of its first NS4A antagonist, ACH-806. While significant reductions in HCV viral load were observed even at the lowest doses studied in a human proof-of-concept trial (graphic above, right), unacceptable levels of serum creatinine, a key marker of kidney function, were also observed. As a result, Achillion, along with its partner Gilead Sciences, made the decision to discontinue development of the compound and focus efforts on the next series of NS4A antagonists, including ACH-1095. Importantly, these trial data validated NS4A as a novel therapeutic target for the treatment of HCV by demonstrating human clinical activity against the virus.

**A Phase 1b/2 study in HCV genotype 1-infected individuals provided the first demonstration of human antiviral activity of a first-generation NS4A antagonist for HCV.**

**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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