

## Hepatitis C Treatments in Current Clinical Development

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There are many potential targets being pursued by drugs treating HCV. A number of compounds for these targets are in early “test-tube” development or pre-clinical “animal” development phases. Most of these compounds, however, will never make it to trials in humans (clinical studies). In fact, only one in 1,000 compounds makes it to human testing. Of those drugs that make it to human testing only 1 in 5 will receive FDA marketing approval. Therefore, every effort has been made to focus this list only on treatments that are known to be in current active clinical development.

When a company is ready to proceed to clinical trials, it files an Investigational New Drug Application (IND) with the Food and Drug Administration (FDA). Most clinical trials are designated as phases I, II, or III, and sometimes IV based on the type of questions that the study is seeking to answer.

### Study Phases:

- In *Phase I* clinical trials, researchers test a new drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
- In *Phase II* clinical trials, the study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.
- In *Phase III* studies, the study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.
- In *Phase IV* studies, the drug is already on the market for a particular indication, but is now being tested for a different indication, use, or disease.

*The following table will be updated as clinical developments move forward:*

### Quick reference chart:

Phase I	Phase II	Phase III	Phase IV
	ANA 245	REBIF	Infergen
Oral Interferon alpha	HepX™-C	IP-501	Amantadine
VX 950	Rituximab (Rituxam)	Viramidine	
JTK 003	NM283	Zadaxin	
R803	ISIS 14803		
HCV/MF59	E-1		
SCH-6	Civacir		
HCV-086	Merimebodib- VX-497		
	Interferon gamma-1b		
	Interleukin-10		

	Omega Interferon		
	Multiferon		
	BILN 2061		
	IDN-6556		
	Ceplene		

**Table of Hepatitis C Drugs in Current Clinical Development**

<b>Drug Name</b>	<b>Drug Category</b>	<b>Pharmaceutical Company</b>	<b>Clinical Phase</b>
<b>HCV-086</b>		<b>ViroPharma/Wyeth</b>	<b>Phase I</b>
<b>Albuferon</b>	Longer Acting Interferon	Human Genome Sciences	<b>Phase I</b>
<b>Comments:</b> Fusion of the genes for human interferon and albumin. Interim results of phase I/II studies demonstrate that it is well-tolerated, has a long half-life (up to 158 hours), and is biologically active in adults with chronic HCV.			
<b>Oral Interferon alpha</b>	Oral Interferon	Amarillo Biosciences	<b>Phase I</b>
<b>Comments:</b> Testing low dose oral administration of alpha interferon absorbed through mucosal membranes.			
<b>VX-950</b>	Protease Inhibitor	Vertex	<b>Phase I</b>
<b>Comments:</b> VX 950 has demonstrated good cellular activity in two assays. The anti viral activity can be sustained in viral clearance assays resulting in a continuing decline of HCV RNA for 9 days. Phase I studies expected to begin in 2004.			
<b>JTK 003</b>	Polymerase Inhibitor	AKROS Pharma	<b>Phase I</b>
<b>Comments:</b> Inhibits HCV genotype 1 polymerase.			
<b>R803</b>	Non-nucleoside HCV Polymerase Inhibitor	Rigel Pharmaceuticals	<b>Phase I</b>
<b>Comments:</b> Clinical data indicates that R803 is well tolerated with no notable adverse effects reported in the dose levels that Rigel plans to use moving forward. Phase I/II efficacy trials for the U.S. planned to commence during the second quarter of 2004.			
<b>HCV/MF59</b>	Vaccine	Chiron	<b>Phase I</b>
<b>Comments:</b> In collaboration with CSL Ltd. and St. Louis University.			
<b>SCH-6</b>	Serine Protease	Schering	<b>Phase I</b>
<b>Comments:</b> In tests it was found the SCH-6 could protect the cell's defenses and actually may prevent the HCV virus from blocking the immune response and restoring body's natural antiviral response.			
<b>ANA245</b>	Isatoribine	ANADYS	<b>Phase I/II</b>

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
<p><b>Comments:</b> Interim results of the Phase 1B clinical trial show that isatoribine is biologically active in adults with chronic HCV infection and results from dosing a cohort of six HCV infected patients with 800mg of isatoribine showed a statistically significant reduction of viral load (p=0.03) at the end of one week, with a median change in viral load from baseline of -0.94 log<sub>10</sub> units. Anadys is currently enrolling patients for an isatoribine Phase I/II study.</p>			
<b>Rituximab (Rituxam)</b>	Anti-CD20 Monoclonal Antibody	Genetech/IDEC	<b>Phase I/II</b>
<p><b>Comments:</b> Under investigation for treatment of cryoglobulinemia. Currently approved for non-Hodgkin's lymphoma.</p>			
<b>NM283</b>	Nucleoside Antiviral	Indenix Pharmaceuticals	<b>Phase I/II</b>
<p><b>Comments:</b> In short-term dose escalation studies to evaluate safety and antiviral activity against adults with hepatitis C genotype 1.</p>			
<b>HepX™-C</b>	Monoclonal Antibody	XTL	<b>Phase I/II</b>
<p><b>Comments:</b> Phase I studies on 35 chronic HCV patients indicated good safety and bioactivity. Phase II study of HCV prophylaxis on post liver transplant patients underway.</p>			
<b>IDN-6556</b>	Caspase Inhibitor	Idun Pharmaceuticals	<b>Phase II</b>
<p><b>Comments:</b> Caspase inhibitors do not have any direct antiviral properties, but are believed to preserve the cell structure and protect the liver from damage caused by HCV. Phase I study completed in May 2002 which included patients with stable hepatitis C infection. Data from a Phase 2a clinical trial of an oral formulation of IDN-6556 in patients infected with HCV reported positive safety and tolerability of the drug as well as its ability to reduce elevated aminotransferase (ALT and AST) levels.</p>			
<b>ISIS 14803</b>	Antisense	Isis Pharmaceutical / Elan	<b>Phase II</b>
<p><b>Comments:</b> Genetically inhibits translation (production) of disease-causing proteins. This compound appears to be well-tolerated, with minimal adverse effects. A larger trial combining ISIS 14803 with pegylated/ribavirin is currently underway.</p>			
<b>E-1</b>	Therapeutic Vaccine	Innogenetics	<b>Phase II</b>
<p><b>Comments:</b> Phase III expected 2004-2005. Study results indicated that 38% of patients showed improvement in liver fibrosis score.</p>			
<b>Civacir</b>	Polyclonal Antibody	NABI	<b>Phase II</b>
<p><b>Comments:</b> Prevention of post-transplant recurrence of HCV. Preliminary results show positive safety and pharmacokinetics results.</p>			

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
<b>Merimebodib VX-497</b>	IMPDH inhibitor	Vertex	<b>Phase II</b>
<b>Comments:</b> The preliminary results of a phase II study showed the combination of VX-497, pegylated interferon and ribavirin was safe and well-tolerated, and VX-497 exhibited an anti-viral effect against HCV.			
<b>Interferon gamma-1b</b>	Anti-fibrotic	InterMune	<b>Phase II</b>
<b>Comments:</b> The primary endpoint of the study, reversal of liver fibrosis as determined by the Ishak histology scoring system, was not met. Studies for milder disease and longer duration of therapy are pending.			
<b>Omega Interferon</b>	Interferon	BioMedicine	<b>Phase II</b>
<b>Comments:</b> New formulation intended to target the liver specifically in order to reduce the side effects in other tissues.			
<b>Multiferon—Natural Interferon</b>	Interferon, Long Acting Interferon	Viragen	<b>Phase II</b>
<b>Comments:</b> Company is making long-acting pegylated version of product in cooperation with Valantis.			
<b>Ceplene</b>	Histamine	Maxim	<b>Phase II</b>
<b>Comments:</b> Completed phase II studies. Currently in clinical trials with pegylated interferon.			
<b>BILN 2061</b>	Serine Protease	Boehringer - Ingelheim	<b>Phase II</b>
<b>Comments:</b> Intended to block viral replication. Shows dramatic decrease in HCV viral load with only 48 hours of therapy. One of the most promising potential new HCV therapies. However, phase II trials were put on hold until potential toxicities seen in monkeys taking high doses are resolved.			
<b>REBIF Interferon beta-1a</b>	Interferon	Ares-Serono	<b>Phase III</b>
<b>IP-501</b>	Anti-fibrotic	Indevus	<b>Phase III</b>
<b>Comments:</b> Anti-fibrotic agent to treat/prevent cirrhosis. Seems to stimulate collagenase to breakdown collagen—a component of scar tissue.			
<b>Viramidine</b>	Nucleoside Analogue	Valeant Pharmaceuticals Int'l	<b>Phase III</b>
<b>Comments:</b> Pro-drug that results in a version of ribavirin that specifically targets liver cells. Phase I clinical trial results showed that doses up to 1200 mg are safe and well tolerated in humans, and that the amount of viramidine in red blood cells is about half that			

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
after ribavirin dosing. This suggests the potential for less hemolytic anemia than is usually seen with ribavirin. Company recently announced they would commence phase III clinical trials.			
<b>Zadaxin</b> (thymosin alfa-1)	Immunomodulator	SciClone	<b>Phase III</b>
<b>Comments:</b> Boosts the immune system. Use in combination with interferons. Initial results from several clinical trials look encouraging when used in combination with pegylated interferon plus ribavirin.			
<b>Infergen</b>	Interferon, Long Acting Interferon	InterMune	<b>Phase IV</b>
<b>Comments:</b> PEG-Alfacon (Interferon alfacon-1) is a long acting version of Infergen. In January 2003, InterMune announced that it has initiated a Phase I clinical trial as a potential new treatment for HCV.			
<b>Amantadine</b>	Broad Antiviral Agent	Endo Labs Solvay	<b>Phase IV</b>
<b>Comments:</b> Anti-flu agent on the market. Has shown mixed results of efficacy in combination with interferons.			

*Recently cancelled clinical trials:*

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
<i>Heptazyme</i>	<i>RNA inhibitor</i>	<i>RPI</i>	<b><i>Studies Cancelled</i></b>
<i>Levovirin</i>	<i>Nucleoside Analogue</i>	<i>Valeant Pharmaceuticals Int'l</i>	<b><i>Studies Cancelled</i></b>
<i>Interleukin-10</i>	<i>Anti-fibrotic</i>	<i>Schering-Plough</i>	<b><i>Studies Cancelled</i></b>

*The listing of the pharmaceutical industries are for information only and do not constitute endorsement of the pharmaceutical companies or the drugs in development.*