

Hepatitis C Treatments in Current Clinical Development

Alan Franciscus
Editor-in-Chief

There are many compounds being studied to treat hepatitis C. 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 or very near to active clinical development in human subjects.

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 evaluate safety, optimal dose, and may include some information on the drug’s effectiveness. Most drugs that enter phase II studies do not progress on to phase III studies. This is because the drug is being tested in more people for a generally longer period of time so lack of effectiveness and a better picture of the effectiveness emerges.
- 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 to answer questions about sub-populations of the same condition it is approved to treat, or for a different indication, use, or disease.

The testing of new drugs is a long process that typically takes about 12 years from pre-clinical testing to FDA approval and marketing to the general public.

Fast Track Status:

A drug can be granted fast track status by the Food and Drug Administration to help facilitate the development and to expedite the review process of new drugs that have the potential to address an unmet medical need for serious or life-threatening conditions such as hepatitis C.

Orphan Drug Status:

A status given to a certain drug by the Food and Drug Administration to encourage the development of drugs that are necessary, but are too expensive or unprofitable to develop under regular circumstances. Drugs being developed to treat orphan diseases (low prevalence in the population) offer tax reductions and marketing exclusivity for the drug manufacturer (up to 20 years).

For more information about clinical trials for the treatment of hepatitis C go to www.clinicaltrials.gov.

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Clinical Trials – Timeline for new drug development

	Preclinical Testing	Phase I	Phase II	Phase III	FDA	Total Years	Phase IV
Years	3.5	1	2	3	2.5	12	Post-marketing
Test Population	Laboratory & animal studies	20 to 80 healthy volunteers	100 to 300 patient volunteers	1000 to 3000 patient volunteers	Review process/ Approval		
Purpose	Assess safety and biological activity	Determine safety and dosage	Evaluate effectiveness, look for side effects	Verify effectiveness, monitor adverse reactions from long-term use			

Success Rate	5,000 compounds evaluated	5 enter trials		1 Drug approved	
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Source: www.allp.com

The following tables will be updated as clinical developments move forward:

Drugs in Current Clinical Development

Specifically targeted antiviral therapy for HCV (STAT-C) Combinations

Drug Name / Category	Drug Name / Category	Pharmaceutical Company	Clinical Phase
RG7128 (Polymerase Inhibitor)	RG7227 (ITMN-191) Protease Inhibitor	Roche in collaboration with Pharmasset & InterMune	Phase I

Comments: This is the first clinical trial of two direct HCV antiviral medications **without** interferon and ribavirin. In April 2009 the results of a phase I study were released that found that the combination dosing for 14 days produced a median reduction of HCV RNA of -4.8 to -5.2 log₁₀ IU/ml in the highest doses; all doses of the combination produced HCV RNA reductions in 63% of the trial participants (less than 40 IU/mL). The drugs were well-tolerated over the 14 day dosing period with no serious treatment-related serious adverse events, dose reductions or discontinuations. It was also found that there were no drug-drug interactions. The study is being expanded to test additional dosing schedules and in people who were previously treated with interferon but did not achieve an SVR.

AASLD 2009: Results from 13 days of treatment with RG7128 & RG7227: 63% (5 out of 8) genotype 1 treatment-naive patients were HCV RNA negative (<15 IU/mL) and 25% (2 out of 8) of null responders were HCV RNA negative (<15 IU/mL). The drugs were well-tolerated; no treatment discontinuations due to side effects. Special Presentation [Click Here](#).

On November 17, InterMune said an independent data monitoring committee recommended that the company stop testing the therapy in the RG7227 900 milligram dosage given once every 12 hours after three patients had elevated levels of ALT, a liver enzyme.

INFORM-2 (RG7128 & RG7227) is expected to be initiated in the first quarter of 2010 and will also include an arm with ritonavir-boosted RG7227. *(January 12, 2010)*

HCV Inhibitors

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
IDX-375	Polymerase Inhibitor	Idenix	Phase I
<p>Comments: Six healthy subjects received 5 doses (25 mg once daily (QD), 50 mg QD, 100 mg QD, 200 mg QD AND 200 mg twice a day or placebo; IDX-375 was generally safe and well-tolerated. The trial is on-going and Idenix is planning additional studies. <i>(January 12, 2009)</i></p>			
ABT-072	Polymerase Inhibitor	Abbott	Phase I
<p>Comments: In HCV genotype 1 treatment-naive patients ABT-072 given for 2 days resulted in a mean viral load decrease of -1.5 log₁₀. The drug was generally safe and well-tolerated. The authors stated that the results of the trial supported the continued development of ABT-072 and that it has the potential of a once a day dose. <i>(December 09, 2009)</i></p>			
Clemizole	NS4B Inhibitor	Eiger BioPharmaceuticals	Phase I
<p>Comments: On August 11, 2009 it was announced that a proof of concept study will be launched to test clemizole in HCV treatment-naive genotype 1 & 2 patients. <i>(August 13, 2009)</i></p>			
ACH-1625	Protease Inhibitor	Achillion	Phase I
<p>Comments: On June 29, 2009, it was announced that a phase I study of ACH-1625 began dosing in healthy and HCV positive patients to test the safety, tolerability, pharmacokinetic and antiviral properties. The trial is expected to enroll approximately 54 subjects. On September 28, 2009, Achillion announced that it had completed the above enrollment and has begun dosing in a phase 1b study of HCV patients.</p> <p>The preliminary results from the phase 1b proof of concept study found that ACH-1625 achieved a mean viral load reduction of 3.94 log₁₀. It was also reported that the the drug continued to show good safety and tolerability.</p> <p>On January 11, 2010 Achillion announced that in a dosing cohort of 9 patients (6 received ACH-1625; 3 received placebo) there was a mean 4.25 log₁₀ reduction of HCV RNA. Achillion stated that the safety results were similar to the safety in the previous dosing group. <i>(January 12, 2010)</i></p>			
MK-3281	Polymerase Inhibitor	Merck	Phase I
<p>Comments: AASLD 2009: Results from a small study of 22 HCV treatment-naive and treatment-experienced patients. In the genotype 1b group there was found to be a 3.75 log₁₀ decrease in HCV RNA. No serious side effects were reported. <i>(November 06, 2009)</i></p>			
PSI-7851	Polymerase Inhibitor	Pharmasset	Phase I

Comments: AASLD 2009: In a multiple dose (50mg, 100mg, 200mg or 400mg) study of treatment-naive HCV genotype 1 patients (40 patients) treated for 3 days PSI-7851 was well-tolerated. The dose-dependent HCV RNA decline was up to 1.95 log₁₀ IU/mL. Additional studies of PSI-7851 in combination with pegylated interferon plus ribavirin are being planned. *(November 6, 2009)*

ABT-450 HCV

Protease Inhibitor

[Abbott / Enanta](#)

Phase I

Comments: In a study of healthy volunteers, ABT-450 at 200mg (once-a-day dosing) in combination with ritonavir (boosting) demonstrated good blood exposure or levels of the study drug. *(December 09, 2009)*

BI 201335

Protease Inhibitor

[Boehringer Ingelheim
Pharma](#)

Phase I

Comments: AASLD 2008: A small study of 19 prior HCV genotype 1 treatment-experienced patients were divided into three groups and were given once-a-day dosing of either 48, 120 or 240 mg of BI 201335 a day in combination with pegylated interferon and ribavirin for 28 days. The drug was found to produce a virologic response in all treatment doses through day 28. The higher dose of 240 mg/day produced the highest virologic response. There were no serious side effects reported – the side effects experienced were consistent with the side effects seen in pegylated interferon plus ribavirin therapy. One patient discontinued treatment due to anxiety. Boehringer announced that further development is being planned. *(February 10, 2009)*

VX-813

Protease Inhibitor

[Vertex](#)

Phase I

Comments: Vertex has announced that they have initiated a Phase I study. *(October 28, 2008)*

PHX1766

Protease Inhibitor

[Phenomix](#)

Phase I

Comments: AASLD 2009: In a study of healthy volunteers and HCV genotype 1 patients given PHX1766 the average maximal HCV-RNA decline observed in 6 days was 1.2 log in the 400mg BID group and 1.8 log₁₀ in the 800mg BID group. PHX1766 was generally well-tolerated. One serious adverse event was reported but the authors stated that it was unrelated to the study drug. *(November 6, 2009)*

ABT-333

Polymerase Inhibitor

[Abbott](#)

Phase I

Comments: On June 11, 2008, Abbott announced the initiation of a Phase I study to test the safety, tolerability, antiviral activity and pharmacokinetics of ABT-333 in healthy volunteers and in HCV positive individuals.

EASL 2009: In a study of healthy adults ABT-333 was found to safe and generally well-tolerated in doses of 200, 400, 600, and 100 mg BID (twice a day) when given for 10 days. *(May 5, 2009)*

AASLD 2009: In all the groups who were treated with ABT-333 plus Peg/ribavirin—at Day 28

41.7% (10 out of 24 patients) had less than 25 IU/mL HCV RNA compared to 0% (0 out of 6 patients) in the placebo group (without ABT-333). The side effects were reported to be mild in severity (85%) with 63% believed to be from Peg/ribavirin. There were no serious AEs or discontinuations due to AEs. *(November 6, 2009)*

VCH-916

HCV Polymerase Inhibitor

[Vertex](#)

Phase I

Comments: In a small study of healthy volunteers, VCH-916 was found to be generally safe and well-tolerated and achieved plasma concentrations proportional to the dose given. Based on these results a 14-day study of HCV genotype 1 treatment-naïve subjects is being planned.

On March 12, 2009, Vertex announced that it had completed acquisition of ViroChem and will be developing ViroChem's HCV polymerase inhibitors in combination with their drug and will study ViroChem's drugs in combination with pegylated interferon plus ribavirin. *(March 13, 2009)*

**PF-00868554
(Filibuvir)**

HCV Polymerase Inhibitor

[Pfizer](#)

Phase I

Comments: EASL 2009: Week 4 data from a study of 35 patients treated with 200, 300, 500 mg (plus placebo) BID (twice a day) plus pegylated interferon/ribavirin found that up to 75% were viral load negative at week 4. The drug was generally well-tolerated. *(May 5, 2009)*

VX-500

HCV Protease Inhibitor

[Vertex](#)

Phase I

Comments: VX-500 recently began a phase Ib study. Data is expected in the first quarter of 2009. *(February 10, 2009)*

RG7128

Polymerase Inhibitor

[Pharmasset/Roche](#)

Phase I

Comments: AASLD 2008: HCV genotype 2 and 3 prior non-responders were treated with RG7128 (1500 mg twice a day) in combination with Pegasys plus ribavirin for 28 days. There was a mean viral log reduction of 5.0 log₁₀. RG7128 was generally well-tolerated and further development in genotype 2 and 3 patients is being planned.

On January 12, 2009, Pharmasset announced the FDA approval of a phase 2b study of RG7128 in combination with Pegasys and ribavirin. The study is expected to enroll 400 HCV genotype 1 or 4 treatment-naïve patients. The study subjects will be enrolled into 4 arms – RG7128 (500 or 100mg bid) plus Pegasys and ribavirin for a treatment durations of 24 or 48 weeks and one control arm – Pegasys plus ribavirin – for a treatment duration of 48 weeks.

On April 25, 2009, it was announced that the first patient had been dosed.

On November 24, 2009, Roche announced that it would open up enrollment for the remaining 300 patients. *(December 14, 2009)*

IDX184	Polymerase Inhibitor	Idenix	Phase II
<p>Comments: AASLD 2009: Data from a three-day, phase I proof-of-concept study evaluating the safety and antiviral activity of IDX184 (monotherapy) enrolled 41 treatment-naive HCV genotype 1-infected patients into four dosing cohorts (25 mg, 50 mg, 75 mg and 100 mg). Mean viral load declines ranged from 0.47 log₁₀ in the 25 mg group to 0.74 log₁₀ in the 100 mg group after three days of treatment. IDX184 was well-tolerated in this study with no serious adverse events reported and no discontinuations from the study.</p> <p>Idenix announced that it has begun a phase II study of IDX184 in combination with pegylated interferon and ribavirin. On January 11, 2010 Idenix announced that in the 50 mg group (in combination with pegylated interferon/ribavirin) there was a median change in HCV RNA of -3.66 log₁₀ compared to a -1.70 log₁₀ in the group that received the placebo (plus pegylated interferon/ribavirin). <i>(January 12, 2010)</i></p>			
RG7227 (formerly ITMN-191)	Protease Inhibitor	InterMune/Roche	Phase II
<p>Comments: On September 2, it was announced that InterMune, according to the agreement with Roche, had met certain milestones and that further clinical development would be transitioned over to Roche.</p> <p>Roche announced on August 19, 2009 the initiation of a Phase II clinical trial of RG7227 (ITMN-191) in combination with Pegasys and ribavirin to study safety, tolerability and effectiveness. The study will enroll about 300 patients in 45 global sites. On September 29th it was also announced that a separate study would evaluate the boosting properties of ritonavir when used with the combination of RG7227 (ITMN-191), Pegasys plus ribavirin.</p> <p>It was announced on January 12, 2010 that, for the 15-day study of 100 mg (twice daily) RG7227 along with low dose ritonavir as a booster medication (plus pegylated interferon/ribavirin) or once daily 200mg, the majority of patients were found to be HCV RNA negative by the end of the study period. There were no drug-related adverse events reported. InterMune expects to start a phase 2b triple combination study in the third quarter of 2010. The un-boosted part of the on-going phase 2b study is being terminated. <i>(January 12, 2009)</i></p>			
ANA598	Polymerase Inhibitor	Anadys Pharmaceuticals	Phase II
<p>Comments: On December 1, 2008 ANA598 received <u>fast-track designation</u> from the FDA</p> <p>EASL 2009: It was reported that ANA598 produced rapid and sustained reductions in HCV RNA with median reductions at the end of treatment (Day 4) exceeding 2 log₁₀ (>99%) at all dose levels. At 200 mg bid (twice-daily) the median viral load reduction was 2.4 log₁₀ (range of 0.4 to 3.4); at 400 mg bid, 2.3 log₁₀ (range of 1.6 to 3.5); and at 800 mg bid, 2.9 log₁₀ (range of 2.2 to 3.4). Genotype 1a patients demonstrated median reductions of 1.4 log₁₀, 1.8 log₁₀, and 2.5 log₁₀ at 200, 400 and 800 mg bid, respectively. In 10 of the 12 genotype 1a patients who received ANA598, viral load was still declining at the end of the three days of treatment. Genotype 1b patients demonstrated median reductions of 2.6 log₁₀, 2.5 log₁₀, and 3.2 log₁₀, at 200, 400 and</p>			

800 mg bid, respectively. In a separate study of healthy volunteers (14 day study) three people developed a severe rash and discontinued therapy.

It was announced on July 31, 2009 that Anadys received FDA clearance to start a phase II study in 90 HCV genotype 1 treatment-naïve patients for a dose finding study – First day 800 mg bid followed by 200 or 400 mg, twice daily or placebo in combination with pegylated interferon plus ribavirin for 12 weeks followed by pegylated interferon plus ribavirin for a total treatment duration of 24 or 48 weeks.

Interim data from the Phase II study showed that 56% of patients treated became HCV undetectable after four weeks of treatment with ANA598 in combination with pegylated interferon and ribavirin compared to 20% in those who were treated with placebo, pegylated interferon plus ribavirin (without ANA598). (*December 18, 2009*)

MK-7009

HCV Protease Inhibitor

[Merck](#)

Phase II

Comments: EASL 2009: The results of a study of 95 treatment-naïve patients with HCV genotype 1 who were randomized into 5 groups (300 & 600 twice a day; 300 & 600 once-a-day; and one placebo group Peg/riba only) were presented. All dosages of MK-7009 were found to have potent antiviral effects and were generally well-tolerated with no serious adverse events or discontinuations.

AASLD 2009: Updated information about the on-going trial (above) was presented. The proportion of subjects who achieved RVR in the MK-7009-containing arms ranged from 69% to 82%, vs. 6% in the placebo group and the percentage of patients who achieved an EVR ranged from 76 to 89% compared to 60% in the placebo group. No serious adverse events resulted in treatment discontinuation. (*November 6, 2009*)

BI 207127

Polymerase Inhibitor

[Boehringer Ingelheim](#)

Phase II

Comments: AASLD 2009: In a small trial of 60 HCV genotype 1 patients, BI 207127 was found to be a potent inhibitor of viral replication in monotherapy, causing a steep decline of viral load at 800 mg every 8 hours in the first 24 hours (5/9 patients with >4 log₁₀ reduction at Day 5, no viral load breakthroughs). BI 207127 was generally safe and well-tolerated in this study; the only drug-related severe adverse event, a moderate erythema (red skin/rash), was managed effectively. Two other cases of mild transient rash did not require BI 207127 dose reduction or discontinuation. A 4-week combination study with doses of BI 207127 up to 800 mg three times a day in combination with pegylated interferon and ribavirin will be completed in the 4th quarter of 2009. (*November 6, 2009*)

A-832

NS5A Inhibitor

[ArrowTherapeutics](#)

Phase II

Comments: A-832 is a NS5A inhibitor that was found (in a test tube) to prevent the HCV IRES-dependent translation process. A phase I study of A-831 has been initiated in healthy volunteers. In 2007, AstraZeneca acquired Arrow Therapeutics, Ltd. There has been no further news about the development of A-831. (*February 10, 2009*)

GS 9190	Polymerase Inhibitor	Gilead	Phase II
<p>Comments: Gilead has begun recruitment for a clinical trial to study the safety, tolerability and effectiveness of GS-9190 in combination with Pegasys plus ribavirin for a treatment duration of 24 or 48 weeks. <i>(February 10, 2009)</i></p>			
BMS-790052	NS5A Inhibitor	Bristol-Myers Squibb	Phase II
<p>Comments: In a phase I study of healthy volunteers, BMS-790052 was found to be safe and well-tolerated and the absorption and distribution properties of the drug appeared to suggest a once-a-day dosing. In a study of HCV genotype 1 patients it was found to produce a rapid reduction in HCV RNA in the 1, 10, and 100 mg doses. BMS is currently recruiting patients for a phase II study in HCV genotype 1 treatment non-responders and naive patients. BMS-790052 will be dosed from 1-100 mg (once or twice a day). <i>(January 26, 2009)</i></p>			
SCH900518 (Narlaprevir)	Protease Inhibitor	Schering / Merck	Phase II
<p>Comments: On November 24, 2008 Schering announced the results from a Phase I clinical trial of Narlaprevir in treatment-naïve patients and HCV patients who did not respond to a previous course of HCV treatment. SCH518 was given as either monotherapy or in combination with peginterferon and demonstrated enhanced antiviral activity, with up to 4log₁₀ and 5log₁₀ decreases in HCV RNA respectively. A phase IIa study is currently on-going, but no further details have been released.</p> <p>On March 9, 2009, it was announced that Merck would buy Schering-Plough. The sale of Schering to Merck is contingent on the approval of Merck and Schering stockholders as well as government regulatory agencies. Merck announced that they expect the transaction will be completed by the end of 2009.</p> <p>AASLD 2009: Narlaprevir with ritonavir (once-a-day) was found to have potent anti-HCV activity. The 200 mg/ 400 mg narlaprevir/ritonavir once-a-day achieved undetectable HCV-RNA levels at week 4 in 58-87% of patients & at week 12 in 84-87% of patients. Narlaprevir/ritonavir was found to be generally safe and well-tolerated. No discontinuations were reported, but there was an increased incidence of anemia in the narlaprevir/ritonavir group compared to the group that did not receive narlaprevir/ritonavir. Studies evaluating 200 mg and 400 mg narlaprevir once-a-day with ritonavir (with and without a lead-in) are currently planned. <i>(November 6, 2009)</i></p>			
VCH-759	Polymerase Inhibitor	Vertex	Phase II
<p>Comments: AASLD 2007: In a 10 day phase I study in which 32 treatment naïve HCV patients received different doses of VCH-759 (400 mg TID, 800 mg BID, and 800 mg TID) all patients achieved a 1 log₁₀ decrease in HCV RNA but the higher dose arm of 800 mg TID achieved 2.5 log₁₀ decrease. The drug was generally well-tolerated. A Phase 2, Multicenter, Randomized, Double-Blinded, and Placebo-Controlled Study of the Antiviral Activity, Safety and Pharmacokinetics of VCH-759 is underway.</p>			

On March 12, 2009, Vertex announced that it had completed acquisition of ViroChem and will be developing ViroChem's HCV polymerase inhibitors in combination with their drug and will study ViroChem's drugs in combination with pegylated interferon plus ribavirin. (*March 13, 2009*)

ITX5061

HCV Entry Inhibitor

[iTherx](#)

Phase IIa

Comments: iTherx will commence a phase 2a study that will enroll 40 patients (European study sites) to test ITX5061 as a single agent for viral load reductions, safety and tolerability. (*February 9, 2009*)

TMC435

Protease Inhibitor

[Medivir/Tibotec](#)

Phase IIa

Comments: TMC435 (formerly TMC435350-C201) is a phase IIa proof-of-concept, blinded, randomized, placebo-controlled trial to assess the effectiveness, safety, tolerability, and pharmacokinetics of four different dose regimens of TMC435350 (25 mg daily, 75mg daily, 200mg daily, 400mg daily). 96 treatment-naïve and 24 treatment-experienced patients with chronic genotype-1 HCV infection will be enrolled in the trial which will be conducted at more than 20 sites in Europe. Patients will receive either TMC435350 or placebo once daily (qd) for 28-days. Standard of Care (SoC) treatment, peginterferon alpha-2a (Pegasys®) and ribavirin (Copegus®), will be provided for 48 weeks or, optionally, for 24 weeks for those patients with an undetectable HCV viral load at Week 4 and who remain undetectable at Week 20. Patients will be followed-up for 24 weeks after the end of standard of care (Peg/ribavirin) to allow evaluation of sustained virologic response (SVR).

EASL 2009: TMC435 given to HCV genotype 1 treatment-naïve patients at doses of 25, 75 or 200 mg qd (once a day) for 4 weeks was generally well tolerated and showed impressive viral load reductions. The trial in treatment experienced-patients is ongoing.

In another study of 37 HCV genotype 1 treatment-experienced patients, the triple combination of TMC435 plus Pegasys and ribavirin was found to produce strong antiviral activity and to be safe and well-tolerated.

AASLD 2009: A study of prior non-responders and treatment-experienced patients found that at Day 28, all four patients who completed treatment achieved HCV RNA <25 IU/mL with an overall mean change from baseline of 5.86 log₁₀ IU/mL. Three of those four patients had HCV RNA below the lower limit of detection (<10 IU/mL) at Day 28. (*November 6, 2009*)

Boceprevir

(SCH 503034)

Protease Inhibitor

[Schering](#)

Phase III

Comments: On May 21, 2008, Schering announced that they would begin 2 phase III studies to evaluate boceprevir in combination with PegIntron plus ribavirin in treatment-naïve and treatment-experienced patients. The trial will include treatment-naïve and treatment-experienced patients and will be guided by rapid viral response using lead-in strategies and total treatment durations (28 or 36 treatment duration).

On January 27, 2009 Schering Plough announced that it had completed enrollment in their Phase III (HCV SPRINT-2 study).

On March 9, 2009 it was announced that Merck would purchase Schering-Plough. The acquisition must first be approved by the Merck and Schering stockholders and they expect the transaction to be completed by the end of 2009.

EASL 2009: The 5 arm phase II study of boceprevir was completed, The arm that included 103 patients achieved an SVR of 75% – this regime included a 4 week lead-in phase of PegIntron plus ribavirin followed by triple combination therapy of boceprevir, PegIntron and ribavirin for 44 weeks. Total duration of treatment was 48 weeks. The side effects in the boceprevir arms were similar to side effects that are usually seen in pegylated interferon and ribavirin except there was a higher incidence of anemia—about 50% in the boceprevir arms vs. about 33% in the group without boceprevir.

AASLD 2009: Two retrospective analyses of the SPRINT-1 data were conducted:

1. A small study with two arms that included 206 patients: In one arm, patients who were considered null-responders to a PegIntron plus ribavirin 4-week lead-in phase were given boceprevir/PegIntron/ribavirin for an additional 44 weeks and 55% (12 out of 22 patients) achieved SVR.
2. In people who achieved RVR after 4 weeks of triple therapy the SVR rate was 82% in the 28 week treatment arm and 94% in the 48 week treatment arm. (*November 13, 2009*)

Telaprevir (VX 950)	Protease Inhibitor	Vertex	Phase III
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Comments: On January 23, 2008, Vertex announced that they will begin recruitment into a phase III clinical trial in March 2008. The ADVANCE trial will be conducted in about 100 centers in the U.S., Europe and certain other countries. The study will enroll approximately 1050 HCV genotype 1 treatment naïve patients. There will be 3 treatment arms comparing telaprevir in combination with pegylated interferon plus ribavirin for a treatment duration of 24 weeks. The control arm will be patients treated with pegylated interferon plus ribavirin for 48 weeks (current standard of care). This is the pivotal Phase III study that will be used to apply for FDA marketing approval, which Vertex expects to seek in late 2010.

On October 15, 2008 Tibotec (Vertex's European Partner) announced that it has begun enrollment into its phase III study called REALIZE to evaluate telaprevir in combination with pegylated interferon plus ribavirin in prior treatment null responders, partial responders, and relapsers. The study will enroll about 650 treatment experienced HCV patients in the US, Europe and other countries throughout the world.

Phase II Clinical Trials:

PROVE 2: The study results of 323 HCV genotype 1 treatment-naïve patients (never been treated) was released at this year's (2008) AASLD conference. The results found that the arm that received the 24 weeks of treatment (12 weeks of telaprevir plus pegylated interferon plus ribavirin followed by 12 weeks of pegylated interferon plus ribavirin (without telaprevir) had the highest SVR rate – 69% (56 out of 81 patients) compared to 46% (38 out of 82 patients) in the arm that received 48 weeks of pegylated interferon plus ribavirin (control arm).

EASL 2009:

PROVE3 data of 453 patients who did not achieve a sustained virological response (SVR) with a previous course of pegylated interferon plus ribavirin was released. Non-responders by type of

non-response was: non-responders (38-39%); relapsers (69-76%); viral breakthroughs (51-52%).

AASLD 2009:

PROVE3: SVR24 result were found to be identical to the SVR12 rates except one person was lost to follow-up.

Study 107: Interim results from an on-going study of people who failed to achieve an SVR with a previous course of pegylated interferon plus ribavirin therapy was released at AASLD and found that 24 week response rates were null-responders (57%), partial responders (55%), relapsers (90%), and viral breakthroughs (75%). The safety profile is consistent with other studies of telaprevir, pegylated interferon and ribavirin.

Study C208 is a new study that is evaluating different doses of telaprevir – 750 mg every 8 hours (q8h or three times a day) compared to 1125 mg dose every 12 hours (q12h or twice a day) in HCV genotype 1 treatment-naïve patients. Week 12 data found that 81-85% of patients who received the every 8 hour dose were HCV undetectable compared to 82.1 to 82.5% in the group that received the every 12 hour dose. *(December 14, 2009)*

Drugs in Clinical Development (General)

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
SCY-635	Cyclophilin Inhibitor	SCYNEXIS	Phase I
<p>Comments: The top-line results from a Phase Ib trial of SCY-635 demonstrated that it produced a clinically relevant reduction in HCV RNA and that it was well-tolerated with no serious adverse events, no discontinuations and no dose-limiting toxicities. The highest dose tested (900 milligrams/day) showed clinically relevant antiviral activity.</p> <p>AASLD 2009: According to a company press release data from a phase one study found that SCY-635 demonstrated promising antiviral activity when combined with HCV polymerase and protease inhibitors. A phase 2 study is expected to begin in the second quarter of 2010. <i>(November 6, 2009)</i></p>			
ANA773	TLR Agonist	Anadys Pharmaceuticals	Phase I
<p>Comments: Andays announced that they had begun oral dosing of ANA773 in people with chronic hepatitis C. The study will evaluate the safety and tolerability of ANA773 in doses of 800, 1200, 1600 and 200 mg given to patients every other day for 28 days.</p> <p>AASLD 2009: ANA773 demonstrated a substantial antiviral response in HCV patients at 1600 & 2000 mg. Two out of 6 patients in the 1600 mg group and 5 of 8 in the 2000 mg group had a maximal decline > 1 log₁₀. No serious adverse events or early discontinuations were reported. <i>(November 6, 2009)</i></p>			

CYT107	Immunomodulator	Cytheris	Phase I
<p>Comments: A study to evaluate the safety and tolerability of CYT107 in combination with pegylated interferon and ribavirin has begun enrolment in Taiwan, France, Italy and Switzerland. <i>(October 28, 2008)</i></p>			
SPC3649 (LNA-antimiRTM-122)	microRNA	Santaris Pharma	Phase I
<p>Comments: On May 29, 2008 Santaris announced that it was commencing a study of SPC3649 in up to 48 healthy male volunteers who will receive SPC3659 or placebo. The trial is a placebo-controlled, double-blind, randomized, single dose, dose-escalating safety study. After establishing the safety and tolerability of the drug the next step would be to study the drug in HCV patients. MicroRNA drugs are a new class of drugs and this trial is the first to test a microRNA in humans. It was announced that the phase I trial was completed in May 2009. <i>(May 5, 2009)</i></p>			
CF102	A3AR Agonist	CAN-FITE	Phase I
<p>Comments: Can-Fite announced the completion of a phase I clinical trial in 25 healthy adults. In addition to determining the dosing range for future studies, CF102 was found to be safe and well-tolerated. A phase I/II study is being planned to study antiviral properties; there is also a separate study of CF102 as treatment for liver cancer. <i>(February 10, 2009)</i></p>			
IMO-2125	TLR9 Agonist	Idera Pharmaceuticals	Phase I
<p>Comments: On September 17, 2007 Idera Pharmaceuticals announced that it started enrollment of patients to study the safety, tolerability and antiviral properties of IMO-2125 in prior null-responder HCV patients. The study is expected to complete enrolment in January 2010.</p> <p>On October 7, 2009 Idera announced that patient treatment has been initiated in a phase 1 clinical trial evaluating IMO-2125 in combination with ribavirin in treatment-naive patients with chronic hepatitis C virus (HCV) infection. IMO-2125 is administered subcutaneously once a week for four weeks in combination with daily oral administration of standard doses of ribavirin. Target enrollment is 15 patients per cohort, with 12 randomized to receive IMO-2125 plus ribavirin and three randomized to receive placebo plus ribavirin treatment. The primary objective of the trial is to assess the safety and tolerability of IMO-2125 over an escalating range of dosages in combination with standard doses of ribavirin. The clinical trial is expected to be conducted at five or more sites in France and Russia.</p> <p>Interim data from the trial above found the drug to be safe and well-tolerated with dose-dependent increases in immune system activation leading to a 40 to 75% (depending on dose) viral load reduction of 1 log₁₀. <i>(December 23, 2009)</i></p>			
Bavituximab (formerly Tarvacin)	Anti-Phospholipid Therapy	Peregrine	Phase I

Comments: On October 10, 2007, Peregrine announced that it had begun dosing the first patient in a trial of bavituximab for treatment of hepatitis C in people with HIV and hepatitis C coinfection. Peregrine expects to enroll 24 patients in the study.

AASLD 2007: In a study of 24 patients who received bavituximab twice weekly in escalating doses based on body weight for two weeks and where the patients were followed another two weeks, it was found that the HCV RNA viral load reductions were in the moderate range of .5 log¹⁰. Bavituximab was found to be generally safe and well-tolerated with no dose limiting toxicities or serious side effects reported. *(November 18, 2007)*

NOV-205

Immunomodulator

[Novelos Therapeutics](#)

Phase I

Comments: A phase I study has begun to evaluate NOV-205 versus placebo as monotherapy in 18 chronic hepatitis C genotype 1 patients who previously failed treatment with pegylated interferon plus ribavirin. Results from the study found that, in the 12 patients treated (6 patients received placebo), there was favorable safety data which has led Novelos to plan a larger study in the second half of 2008 *(December 13, 2007)*

GS-9450

Caspase Inhibitor

[Gilead](#)

Phase II

Comments: **EASL 2009:** GS-9450 was found to be generally safe and well-tolerated in healthy adults. Phase II studies of GS-9450 are currently underway in people with HCV and steatosis *(May 5, 2009)*

CTS-1027

Anti-inflammatory

[Conatus](#)

Phase II

Comments: On December 20, 2007, Conatus announced the initiation of a phase II study of CTS-1027 that will enroll 100 HCV patients for 4 weeks in a proof of concept trial. A second study has been initiated to test the optimal dose of CTS-1027 alone and in combination with ribavirin in up to 70 patients who will be treated for up to 24 weeks. *(July 1, 2009)*

Oglufanide disodium

Immunomodulator

[Implicit Bioscience](#)

Phase II

Comments: A drug that works as a regulator of the body's immune response has begun testing in hepatitis C positive patients. Two studies are currently underway: 1) phase Ib study of Oglufanide by injection, and 2) an intranasal study. *(November 20, 2007)*

Alinia (nitazoxanide)

Thiazolides

[Romark](#)

Phase II

Comments: **AASLD 2008:** A study with a different lead-in time using nitazoxanide in combination with pegylated interferon plus ribavirin was released. A 4 week lead-in of 500 mg twice a day (taken with food) of nitazoxanide was followed by nitazoxanide plus Pegasys for 36 weeks. SVR rates are listed by genotype: 3 of 3 patients with HCV genotype 1 – 100% SVR; 1 of 1 patient with HCV genotype 2 – 100% SVR; and 31 of 40 patients with HCV genotype 4 –

78% SVR. These results compare favorably with another clinical trial of nitazoxanide used in combination with pegylated interferon plus ribavirin that used a 12 week lead-in phase. The 4-week lead-in phase appears to be as effective as the 12-week lead-in phase.

AASLD 2009: Interim results from (ERAIS-C) a study of 23 HCV genotype 1 patients were released and it was found that the addition of NTZ improves RVR. The SVR results are needed to confirm if improved RVR results correlate to higher SVR results.

Interim results from another study of 14 HCV genotype 1 non-responders with cirrhosis found that 50% of patients achieved an EVR of whom 14.3% were undetectable. It appears the addition of NTZ may improve treatment outcomes in this difficult to treat patient group.

Preliminary results from a study of a time-released formulation of NTZ found a dose-related increase in RVR, cEVR and EVR with the combination of NTZ,PEG, RBV in HCV genotype 4 treatment-naive patients. SVR results are pending. (*November 13, 2009*)

SCV-07	Broad Spectrum Immune Stimulator	SciClone	Phase II
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Comments: In a small study of 31 genotype 1 patients treated for 7 days, SCV-07 was found to have antiviral properties against HCV in some patients who received the higher monotherapy doses. (*October 1, 2008*)

MitoQ (mitoquinone)	Inflammation/ Fibrosis Inhibitor	Antipodean Pharmaceuticals	Phase II
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Comments: **EASL 2008:** In a study to determine if MitoQ reduced necroinflammation in 30 patients with hepatitis C it was found that there was a 26.4% (40 mg dose group) and 28% (80 mg dose group) reduction in ALT levels. The drug was well-tolerated with no significant safety issues reported. (*April 29, 2008*)

DEBIO-025	Cyclophilin Inhibitor	Debio	Phase II
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Comments: **EASL 2008:** Results from a double-blind, placebo-controlled study of Debio 025 in combination with Pegasys in HCV genotype 1 and 4 patients vs. treatment with Pegasys monotherapy were released – total of 90 patients in the study. It was found that in the Debio combination arms that there was a 4.6 log₁₀ decrease in HCV RNA in the 600 mg/day arm and a 4.8 log₁₀ decrease in HCV RNA in 1000 mg/day arm. This compares to 2.49 log₁₀ in the Pegasys plus placebo arm and 2.20 log₁₀ decrease in HCV RNA in the Debio 1000 mg/day monotherapy arm.

On January 26, 2009 Debiopharm announced the start of a phase IIb triple therapy study of Debio 025 (60 mg) plus standard doses of Pegasys and ribavirin in 272 HCV treatment-naive genotype 1 patients. (*January 26, 2009*).

PF-03491390 (Formerly IDN-6556)	Pancaspase Inhibitor	Pfizer Pharmaceuticals	Phase II
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Comments: Pancaspase 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. The FDA granted Orphan Drug Designation to PF-03491930 for use with organ transplantation in May 2006.

Study results of doses ranging from 5 mg to 400 mg daily (given 1 to 3 times a day) in 105 patients (with various liver conditions) for 14 days reported in *Hepatology* (August 2007) found that there was a significant reduction of ALT and AST levels in all doses except in the lowest dose group. The study authors concluded that longer studies are needed to assess the potential effects of the drug on liver inflammation and fibrosis. (*August 2, 2007*)

Viramidine (Taribavirin)	Nucleoside Analogue	Valeant Pharmaceuticals Int'l	Phase IIb
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Comments: In two phase III studies viramidine had disappointing rates of effectiveness at the doses given in the clinical trials, but based on the retrospective data of drug exposure in the VISER trials, a new phase 2b study began enrollment of 260 treatment-naïve genotype 1 patients to evaluate taribavirin in doses of 20mg/kg, 25 mg/kg, and 30 mg/kg in combination with pegylated interferon vs. 800-1,400 mg daily ribavirin plus pegylated interferon alfa-2b for 12 weeks. If the data from 12 weeks of treatment is encouraging, Valeant intends to continue the trial for the full 48-week treatment period with a 24 week follow-up period.

Preliminary End of treatment (48 weeks) data from a new Phase IIb study of HCV genotype 1, treatment naïve patients who received taribavirin at 10mg/kg (67 pts), 25 mg/kg (70 pts), and 30 mg/kg (68 pts) per day continues to show viral load reductions similar to the control group of 70 patients who received ribavirin 800-1400 mg daily, but there was a significantly lower rate of anemia in the taribavirin group. (*November 28, 2008*)

Interferons in development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
IL-29 (Type III Interferon)	Long Acting Interferon	ZymoGenetics/BMS	Phase II

Comments: On January 12, 2009, Bristol-Myers announced that it signed an agreement with ZymoGenetics to co-develop IL-29 and will have an option of selling and receiving profits from the sale of IL-29 in the United States as well as royalties from foreign sales.

AASLD 2009: In a study of 25 HCV patients who relapsed to a previous course of treatment and who were given IL-29 and ribavirin (1000-2000 mg) for 4 weeks, it was found that the mean maximum decrease from baseline viral load was 1.8 log₁₀ (0.5-3.6) in the .05 ug/kg group to 3.8 log₁₀ (3.2-5.1) in the 2.25 ug/kg group. In 7 HCV treatment-naïve patients who were given 1.5 ug/kg plus ribavirin for 4 weeks it was found that the maximum decrease in viral load from baseline viral load was 3.3 (1.2-5.5)

On October 27, ZymoGenetics announced they had dosed the first patient in a Phase 2 clinical trial of PEG-Interferon lambda (IL-29) and ribavirin in treatment-naïve patients with chronic

hepatitis C virus (HCV) infection (the “EMERGE” study). *(November 6, 2009)*

Belerofon (oral)	Oral Interferon	Nautilus Biotech	Phase II
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Comments: It was announced on May 14, 2007 that the U.S. Food and Drug Administration approved the initiation of a phase I, open-label, ascending study of four doses of oral Belerofon interferon. According to the company the trial is scheduled to begin in late 2007. *(May 29, 2007)*

BLX-883 (Locteron)	Long Acting Interferon	Biolex Therapeutics / OctoPlus	Phase II
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Comments: A form of interferon being tested with a new technology (LEX System™) for controlled-release of Locteron (injection every two weeks instead of the weekly injection for pegylated interferon).

EASL 2009: In a study of 32 HCV positive people it was found that the severity of side effects was less with locteron compared to the PegIntron group although it is hard to compare because of the small number of patients in the study. The study also found that the antiviral effects of Locteron were similar compared with PegIntron.

It was announced on June 29, 2009 that Biolex has completed enrollment in their SELECT-2 trial of their interferon (320, 480, or 640 ug dose) product that will be dosed once every 2 weeks in combination with ribavirin. The study will compare Locteron plus ribavirin to PegIntron plus ribavirin (control arm). Results are expected in the 4th quarter of 2009. *(July 1, 2009)*

Oral Interferon	Oral Interferon	Amarillo Biosciences	Phase II
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Comments: Amarillo announced that their development partner CytoPharm has been approved to conduct a clinical trial of 165 chronic hepatitis C patients in Taiwan. The aim of the study is to find out if their oral interferon lozenges will help to reduce the relapse rate in patients who will receive a high dose injection of interferon in combination with ribavirin. Results are expected in the 4th quarter of 2010. *(July 1, 2009)*

Omega Interferon	Interferon	Intarcia Therapeutics	Phase II
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Comments: Uses an implantable infusion pump that releases a steady amount of Omega interferon for about 1 month. An ongoing Phase II trial is evaluating daily omega interferon alone and in combination with ribavirin in 102 HCV treatment-naïve patients with genotype 1.

EASL 2007: Final results from this study found that 36% of patients who received daily Omega interferon plus ribavirin achieved an SVR compared to 6% who received Omega interferon monotherapy. The company may study higher doses of Omega interferon. *(April 17, 2007)*

Albuferon (ZALBIN)	Long Acting Interferon (injections every two weeks)	Human Genome Sciences	Phase III
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Comments: Final results of the phase III studies of Zalbin used in combination with ribavirin met its primary endpoint of non-inferiority to Pegasys for treatment of hepatitis C in people with HCV genotypes 1, 2, and 3.

On November 25, 2009 HGS announced that it had submitted an application to the FDA for marketing approval of Zalbin (injection once every 2 weeks & in combination with ribavirin) for the treatment of hepatitis C. (*December 09, 2009*)

Consensus interferon (Infergen)	Interferon	Three Rivers Pharmaceuticals	Phase IV
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Comments: Infergen is being studied in ongoing clinical trials to establish additional labelling for daily use with ribavirin. Enrollment in the Phase 3 trial (DIRECT) was completed in mid-2005 and the trial is expected to be completed in 2007. The DIRECT trial, which should be completed in 2007, is evaluating the safety and efficacy of both 9 mcg and 15 mcg doses of daily Infergen in combination with ribavirin in non-responders.

In December 2006, a phase IV study to treat prior pegylated interferon/ribavirin non-responsive patients began. In this study, patients who are being treated with pegylated interferon plus ribavirin and who remain HCV RNA positive at week 12 will be switched to daily Infergen (15 mcg/day) plus ribavirin (1.0-1.2 g/day) for 36 or 48 weeks or continue on their pegylated interferon and ribavirin regimen for an additional 36 weeks of therapy. Results from the study were released in June 2009 and found that SVR rates were 6.9% in the group that received 9 mcg/day and 10.7% in the group that received 15 mcg/day. (*July 1, 2009*)

Vaccines in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
CT-1011	Therapeutic Vaccine	CureTech/Teva	Phase I
Comments: The first dosing of 20 patients is expected to begin toward the end of 2009. (<i>August 7, 2009</i>)			
MBL-HCV1	Neutralizing Vaccine	MassBiologics	Phase I
Comments: The first dosing of MBL-HCV1 to test the safety and activity of the drug was announced. 30 healthy subjects are expected to be treated. (<i>August 7, 2009</i>)			
ChronVac-C	DNA-based Therapeutic Vaccine	Inovio / Tripep	Phase I
Comments: EASL 2009: The results of a trial of 12 treatment-naïve, HCV genotype patients found that 67% (four out of six patients) in the two highest dose groups had viral load reductions greater than 0.5 log ₁₀ lasting for two to greater than 10 weeks. Of the patients in these groups three had activations of the HCV-specific T cell responses at the time of the viral load reductions indicating an immune response. Samples from 12 patients (HCV genotype 1) found that the vaccine was safe, immunogenic and had transient effects on HCV viral load. (<i>December 09, 2009</i>)			
TG4040	Therapeutic Vaccine	Transgene	Phase I
Comments: EASL 2009: Results from a phase I study found that in 6 out of 15 patients there			

was a decrease in viral load ranging from 0.5 to 1.4 log₁₀ from baseline. All doses were reported to be safe and well-tolerated with no serious adverse events or treatment medication or discontinuation. Transgene reported that a new clinical trial of TG4040 in combination with pegylated interferon plus ribavirin is expected to begin in 2010. (*May 5, 2009*)

PeviPROTM	Therapeutic Vaccine	Pevion Biotech	Phase I
<p>Comments: On December 18, 2006, Pevion Biotech announced the start of a phase I clinical trial in 30 healthy volunteers to test the safety and tolerability of the synthetic vaccine. The secondary objective is to assess the immunogenicity of the vaccine. The study is scheduled for completion by the end of 2007. (<i>September 4, 2007</i>)</p>			
HCV/MF59	Vaccine(s)	Chiron/Novartis	Phase I
<p>Comments: Two vaccines are being tested in collaboration with CSL Ltd. and St. Louis University. Early clinical data from St. Louis University reported that 60 patients received 4 different doses of vaccine, and that all produced HCV antibodies. The study is on-going. (<i>May 2, 2008</i>)</p>			
GI-5005 (Tarmogen)	Therapeutic Vaccine	Globe Immune	Phase II
<p>Comments: A form of therapeutic vaccine that is believed to stimulate the immune system to help fight HCV.</p> <p>On December 19, 2007, GlobeImmune announced the initiation of a phase II study expected to enroll 120 patients who will receive Tarmogen in combination with pegylated interferon plus ribavirin and compare the triple to regular standard of care (peg with ribavirin).</p> <p>AASLD 2009: Report from an ongoing Phase 2b study to compare GI-5005 plus pegylated interferon plus ribavirin versus Peg/riba alone in 140 HCV genotype 1 patients who were either treatment-naïve or prior non-responders. On a modified intent-to-treat basis (patients having received at least one dose of combination therapy), treatment-naïve patients receiving GI-5005 plus Peg/riba as a triple therapy had an end-of-treatment complete response rate (HCV RNA < 25 IU/mL by PCR assay at 48 weeks) of 74%, compared with an end-of-treatment response rate of 59% for treatment-naïve patients receiving Peg/riba (without GI-5005). (<i>November 6, 2009</i>)</p>			
Civacir	Vaccine / Immune Globulin	NABI	Phase II
<p>Comments: A drug that is believed to prevent the post-transplant recurrence of HCV. Preliminary results show positive safety and pharmacokinetics results. On Feb 1, 2006 the FDA granted fast track designation. Initiation of a phase II ‘Proof of Concept’ clinical trial has begun - the Mayo Clinics in Arizona, Florida and Minnesota have started enrollment. On September 11, 2007 Nabi sold its Biologic strategic business (which includes Civacir) to Biotest AG. The close of the transaction is expected by the end of 2007. (<i>November 22, 2007</i>)</p>			
IC41	Therapeutic Vaccine	Intercell	Phase II
<p>Comments: A combination synthetic therapeutic vaccine (medicines to increase the T-cell response plus peptides identified through studies of people with natural immunity to HCV or successful response to HCV therapy).</p>			

IC41 has completed Phase I & Phase II studies and has been shown to have a good safety profile in healthy adults and previously treated HCV patients who failed to achieve a successful treatment outcome. In the HCV patients there was an increase in T-cell response and a temporary reduction of HCV RNA (viral load).

AASLD 2009: Final results: The use of IC41 did not conclusively find a viral load reduction except in the group with a high viral load. *(November 13, 2009)*

Anti Liver Cancer Drugs in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
ALN-VSP	RNAi	Alnylam	Phase I
<p>Comments: On April 2, 2009, Alnylam Pharmaceuticals initiated a Phase I trial, conducted in the U.S., is a multi-center, open label, dose escalation study designed to enroll approximately 55 patients with advanced solid tumors with liver involvement, who have failed to respond to or have progressed after standard treatment. The primary objective is to evaluate the safety, tolerability, and pharmacokinetics of intravenous ALN-VSP, including demonstration of the maximum tolerated dose. <i>(November 20, 2009)</i></p>			
PV-10	Anti-Liver Cancer	Provectus	Phase I
<p>Comments: A phase I study of PV-10 for the treatment of cancer metastatic to the liver or recurrent liver cancer. The study will enroll up to six subjects. <i>(October 05, 2009)</i></p>			
CF102	Anti-Liver Cancer	Can-Fite BioPharma	Phase I/II
<p>Comments: On April 21, 2009 Can-Fite BioPharma announced the initiation of a phase I/II clinical trial testing the safety and effectiveness of CF102 in up to 40 patients. <i>(April 21, 2009)</i></p>			
ZIO-101	Anti-Liver Cancer (Arsenic)	ZIOPHARM Oncology	Phase II
<p>Comments; On May 10, 2007, ZIOPHARM announced the dosing of the first patient in a phase II trial for the treatment of primary liver cancer. This study is not specific to hepatitis C-related liver cancer. <i>(May 29, 2007)</i></p>			
4SC-201 (Resminostat)	HDAC Inhibitor	4SC AG	Phase II
<p>Comments: On August 18, 2009 4SC announced the initiation of a proof of concept study that would test the effectiveness, safety and pharmacokinetics of 4SC-201 used alone or in</p>			

combination with sorafenib (another anti-cancer drug). The study will include two arms (1) 15 patients in a dose escalation study and (2) patients who discontinued sorafenib to be treated with 4SC-201 as a monotherapy. *(September 7, 2009)*

PI-88

Anti-Liver Cancer

[Progen Industries](#)

Phase II

Comments: A treatment for primary liver cancer following surgical resection of a liver tumor. Final results from the phase II clinical trial found that the 160 mg dose was well-tolerated and increased the disease free state (liver cancer) of 25% of the patients and prolonged the time to tumor recurrence from 27 to 48 weeks (78%). Progen estimates that phase III clinical trials will begin at the end of 2007. The U.S. FDA granted Fast Track status and the commission of the European Communities has granted orphan product designation. *(October 1, 2007)*

GV1001 (Heptovax)

Anti-Liver Cancer

[Pharmexa](#)

Phase II

Comments: Initiation of phase II studies has begun in France, Spain and Germany to treat liver cancer (HCC). The trial will enroll 41 patients with advanced liver cancer using GV1001 in combination with GM-CSF (stimulates the production of neutrophils or white blood cells). On November 19, 2007, Pharmexa released interim data on 21 patients in the trial—all six vaccine doses were well-tolerated and no vaccine-attributable serious adverse events were observed. No tumor responses were observed in any of the 21 patients, but the measurable response data will not be available until the second quarter of 2008. *(November 21, 2007)*

**Doxorubicin
(BA-003 Transdrug)**

Anti-Liver Cancer

[BioAlliance Pharma](#)

Phase II

Comments: On December 10, 2009 BioAlliance Pharma announced positive survival data in its phase II clinical trial with doxorubicin Transdrug® in patients with advanced hepatocellular carcinoma (primary liver cancer).

Doxorubicin Transdrug®, a treatment presented in the form of nanoparticles delivered via hepatic intra-arterial route, was granted orphan drug status in Europe and the United States. It is being evaluated in patients with advanced hepatocellular carcinoma.

Phase II results showed a 88.9% survival rate after 18 months of treatment in patients having received three intra-arterial doxorubicin Transdrug® injections, as per protocol. This increased survival rate is relevant compared to the 54.5% rate observed in patients with the current standard of care (usually transarterial chemoembolisation with a cytotoxic drug).

Based on these data, BioAlliance Pharma will design new approaches using doxorubicin Transdrug® while reducing pulmonary adverse events that led to the suspension of the trial. *(December 10, 2009)*

**Doxorubicin
(ThermoDox)**

Anti-Liver Cancer

[Celsion](#)

Phase III

FDA Approved

Comments: Phase one interim results found that ThermoDox (doxorubicin) – heat-activated liposome therapy – in combination with Radiofrequency Ablation of primary and metastatic

tumors to the liver showed local return of cancer in only 2 of 44 tumors resulting in a 4.5% local recurrence rate. Also, 5 of the 10 evaluable patients demonstrated a complete response along with a single partial response. In June 2008 the company also announced a new phase III trial of Doxorubicin in patients with hepatocellular carcinoma (HEAT study).

On December 3, 2009 Celsion reported that enrollment in this 600 patient study continues to accelerate and Celsion expects to meet its objective of completing enrollment by the middle of 2010. A pre-planned, un-blinded interim efficacy analysis will be performed by an independent Data Management Committee when 50% of the endpoint events, tumor recurrence, are realized in the study population. Based on an historical review of RFA cases, Celsion expects the study could be completed by the middle of 2011, and pending positive data, a NDA would be submitted to the FDA before the end of 2011. *(December 10, 2009)*

Nexavar (sorafenib)

Anti-Liver Cancer

[Onyx Pharmaceuticals](#)

Phase IV

Comments: It was announced that Bayer and Onyx have begun enrolment in a multi-international clinical trial to evaluate the use of Nexavar to prevent the recurrence of hepatocellular carcinoma (HCC) following surgery or local radiation for patients with HCC or primary liver cancer. Nexavar is already FDA approved to treat liver and kidney cancer.

On June 1, 2009, Bayer and Onyx announced the initiation of a trial to study the combination of Nexavar and Tarceva (Roche) in patients with liver cancer. The trial is expected to enrol 700 patients with advanced liver cancer to find out if the combination prolongs survival time. *(July 1, 2009)*

Adjunct Therapies

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
LGD-4665	Thrombopoietin Receptor Agonist	Ligand Pharmaceuticals Inc.	Phase II

Comments: A phase I study that evaluated LGD-4665 in multiple doses over 14 days found that it was safe and well-tolerated and produced an increase in platelet counts in the single and multiple daily dose regimens.

In April 2008, Ligand initiated a Phase IIa trial evaluating LGD-4665 in ITP patients in a randomized double-blind, placebo-controlled, proof of concept study. *(December 8, 2008)*

Clinical trials on Hold

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
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None at present			
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Clinical trials that have been cancelled:

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
HEPTAZYME	RNA Inhibitor	RPI	<i>Studies Cancelled</i>
LEVOVIRIN	Nucleoside Analogue	Valeant Pharmaceuticals Int'l	<i>Studies Cancelled</i>
INTERLEUKIN-10	Anti-fibrotic	Schering-Plough	<i>Studies Cancelled</i>
HCV-086		ViroPharma/Wyeth	<i>Studies Cancelled</i>
R803	Non-nucleoside HCV Polymerase Inhibitor	Rigel Pharmaceuticals	<i>Studies Cancelled</i>
IP-501	Anti-fibrotic	Indevus	<i>Studies Cancelled</i>
VX-497 (MERIMEBODIB)	IMPDH Inhibitor	Vertex	<i>Studies Cancelled</i>
BILN 2061	Serine Protease	Boehringer - Ingelheim	<i>Studies Cancelled</i>
SCH-6	Serine Protease	Schering	<i>Studies Cancelled</i>
ANA245	Isatoribine	Anadys	<i>Studies Cancelled</i>
RITUXIMAB	Anti-CD20 Monoclonal Antibody	Genetech/IDEC	<i>Studies Cancelled</i>
JTK 003	Polymerase Inhibitor	Akros Pharma	<i>Studies Cancelled</i>
ISIS 14803	Antisense	Isis Pharma	<i>Studies Cancelled</i>

CEPLENE	Histamine	EpiCept	<i>Studies Cancelled</i>
INTERFERON GAMMA-1B	Anti-fibrotic	InterMune	<i>Studies Cancelled</i>
ANA971	Isatoribine	ANADYS	<i>Studies Cancelled</i>
CPG 10101 (ACTILON)	Immunomodulator	Coley	<i>Studies Cancelled</i>
GS9132/ACH806	Protease Inhibitor	Gilead/Achillion	<i>Studies Cancelled</i>
XTL-2125	Polymerase Inhibitor	XTL Biopharmaceuticals	<i>Studies Cancelled</i>
ANA 975	Isatoribine	ANADYS	<i>Studies Cancelled</i>
AVI-4065	Antisense Compound	BioPharma	<i>Studies Cancelled</i>
UT-231B	Imino Sugar Inhibitor	United Therapeutics	<i>Studies Cancelled</i>
G1262570	Anti-fibrotic	GlaxoSmithKline	<i>Studies Cancelled</i>
EMZ702	Interferon Enhancer	Transition Therapeutics,	<i>Studies Cancelled</i>
INTERFERON BETA-1A (REBIF)	Interferon	Ares-Serono	<i>Studies Cancelled</i>
INNO0101 (E1)	Therapeutic Vaccine	Innogenetics	<i>Studies Cancelled</i>
AMANTADINE	Broad Antiviral	Endo Labs Solvay	<i>Studies Cancelled</i>
R7025 (MAXY-alpha)	Pegylated Interferon	Maxygen/Roche	<i>Studies Cancelled</i>
NM283 (Valopicitabine)	Polymerase Inhibitor	Idenix Pharmaceuticals	<i>Studies Cancelled</i>
HCV-796	Polymerase	ViroPharma/Wyeth	<i>Studies Cancelled</i>

	Inhibitor		
HCV-AB68	Monoclonal Antibody	XTL Bio	<i>Studies Cancelled</i>
XTL-6865 (formerly HepX-C)	Monoclonal Antibody	XTL Bio	<i>Studies Cancelled</i>
Suvus (Methylene blue) formerly BIVN-401 (Virostat)	Antiviral	Genzyme Oncology	<i>Studies Cancelled</i>
Hepaconda	Bezafibrate	Giaconda	<i>Studies Cancelled</i>
R1626	Polymerase Inhibitor	Roche	<i>Studies Cancelled</i>
ZADAXIN® (thymalfasin or thymosin alpha 1)	Immunomodulator	SciClone/Sigma-Tau	<i>Studies Cancelled</i>
GSK625433	Polymerase Inhibitor	GlaxoSmithKine	<i>Studies Cancelled</i>
PYN17	Botanical	Phynova	<i>Studies Cancelled</i>
VGX-410C (Mifepristone)	IRES Inhibitor	VGX Pharmaceuticals	<i>Studies Cancelled</i>
JBK-122	Anti inflammatory	Jenken Biosciences	<i>Studies Cancelled</i>
Eltrombopag (Promacta)	Thrombopoietin Receptor Agonist	GlaxoSmithKline	<i>Studies Cancelled</i>
MX-3253 (celgosivir)	Glucosidase I Inhibitor	MIGENIX	<i>Studies Cancelled</i>

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