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Hepatitis C Treatments in Current Clinical Development

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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.
- 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 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.

For an overview of the latest drug development at AASLD 2007 click [here](#).

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.

[Quick Reference Chart](#)

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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		

Source: www.allp.com

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

Quick Reference Chart

Phase I	Phase II	Phase III	Phase IV	On Hold
HCV/MF59	Oral Interferon alpha	Viramidine	Infergen/Consensus	JBK-122
Bavituximab (Tarvacin)	Civacir	Albuferon	Nexavar	
IL-29 (PEG-Interferon lambda)	Omega Interferon	ZADAXIN® (thymalfasin or thymosin alpha 1)		
NOV-205	PF-03491390 (formerly IDN-6556)	VX 950 (telaprevir)		
ITMN-191	IC41	SCH 503034 (boceprevir)		
R1656	MX-3253 (Celgosivir)	ThermoDox (doxorubicin)		
Belerofon (oral)	VGX-410C			
R7128	DEBIO-025			
A-831	GV1001			
PeviPRO™	PI-88			
PYN17	BLX-883 (Locteron)			
TG4040	MitoQ			
ChronVac-R	SOV-07			
GSK625433	Alinia (nitazoxanide)			
IMO-2125	Z10-101			

LGD-4665	VCH-759			
CF102	Oglufanide disodium			
VCH-916	TMC435350			
VX-500	GI-5005 (Tarmogen)			
PF-00868554	CTS-1027			
SPC3649 (LNA-antimiR TM -122)	Eltrombopag			
ABT-333	SCV-07			
GS 9190	SCH900518 (518)			
ANA598				
IDX184				
CYT107				
PHX1766				
VX-813				
ANA773				
BI 201335				

Drugs in Current Clinical Development

Polymerase/Protease Inhibitors in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
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BI 201335	Protease Inhibitor	Boehringer Ingelheim Pharma	Phase I
<p>Comments: AASLD 2008: In a small study of 19 prior HCV genotype 1 treatment-experienced patients, the 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 best virologic response. There were no serious side effects reported and 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. <i>(November 7, 2008)</i></p>			
VX-813	Protease Inhibitor	Vertex	Phase I
<p>Comments: Vertex has announced that they have initiated a Phase I study. <i>(October 28, 2008)</i></p>			
PHX1766	Protease Inhibitor	Phenomix	Phase I
<p>Comments: Phenomix announced that it had begun enrolling patients in the Netherlands. 24 healthy subjects and 6 HCV patients will be given PHX1766 to test the safety, tolerability and pharmacokinetics. <i>(October 28, 2008)</i></p>			
IDX184	Polymerase Inhibitor	Idenix	Phase I
<p>Comments: On July 29, 2008 Idenix announced the initiation of a phase I study of IDX184 a once-daily oral HCV polymerase inhibitor <i>(August 5, 2008)</i></p>			
ANA598	Polymerase Inhibitor	Anadys Pharmaceuticals	Phase I
<p>Comments: The preliminary results of ANA598 in healthy volunteers found that it was safe and well-tolerated with no serious adverse events. Anadys is planning a phase Ib study of ANA598 in HCV genotype 1 treatment-naïve patients that will include 3 arms with 10 subjects in each arm. Preliminary results from the new study are expected in the first quarter of 2009.</p> <p>On October 28, Anadys began enrollment in a Phase Ib study <i>(October 28, 2008)</i></p> <p>On December 1st, 2008 ANA598 received <u>fast-track designation</u> from the FDA <i>(December 8, 2008)</i></p>			
ABT-333	Polymerase Inhibitor	Abbott	Phase I
<p>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. <i>(June 11, 2008)</i></p>			

VCH-916	HCV Polymerase Inhibitor	Virochem	Phase I
<p>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. <i>(May 21, 2008)</i></p>			
MK7009	HCV Protease Inhibitor	Merck	Phase I
<p>Comments: A phase I double blinded, placebo controlled trial testing the safety and efficacy has been initiated. <i>(May 28, 2008)</i></p>			
PF-00868554	HCV Polymerase Inhibitor	Pfizer	Phase I
<p>Comments: AASLD 2008: Results from a new non-nucleoside inhibitor, PF-00868554, were presented in a poster that reported on the safety, tolerability and pharmacokinetics of this new compound. The study drug was administered to 33 healthy male subjects between 18-55 years old in one of 4 treatment arms. Thirty-one patients finished the study with no serious adverse events, drug discontinuation or dose reductions when the drug was given twice a day for 14 days. The plasma concentrations were as expected, and another study with HCV treatment naïve-patients is currently underway. <i>(November 7, 2008)</i></p>			
VX-500	HCV Protease Inhibitor	Vertex	Phase I
<p>Comments: VX-500 recently began a phase I dose escalation and safety study in healthy volunteers. Vertex expects to begin a trial in HCV patients in mid-2008. <i>(May 28, 2008)</i></p>			
GS 9190	Polymerase Inhibitor	Gilead	Phase I
<p>Comments: AASLD 2007: Results from two parts of a phase I study were released. Part 1: 31 patients treated with single escalating doses of GS 9190, and Part 2: 23 patients received various doses twice daily. Both studies found that GS 9190 was generally well-tolerated and showed antiviral activity against HCV.</p> <p>In these studies there were some concerns over a potential cardiac problem (irregular heart rhythms) so Gilead has initiated another study to determine whether the cardiac problem was caused by GS 9190. If this problem can be resolved, Gilead will advance GS 9190 into larger studies. <i>(November 18, 2007)</i></p>			
GSK625433	Polymerase Inhibitor	GlaxcoSmithKline	Phase I
<p>Comments: Currently recruiting patients to study the initial safety and tolerability in healthy</p>			

adults as well as anti-viral activity. *(September 04, 2007)*

ITMN-191 (R-7227)

Protease Inhibitor

[InterMune/Roche](#)

Phase I

Comments: On May 29, 2008 InterMune announced it has begun dosing of a 14-day phase 1b trial evaluating ITMN-191 in combination with Pegasys and ribavirin (triple therapy) in treatment-naïve genotype 1 patients.

The company also reported that the results from a trial using ITMN-191 in HCV treatment-experienced patients warranted continued development of ITMN-191.

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. *(September 12, 2008)*

R7128

Polymerase Inhibitor

[Pharmasset/Roche](#)

Phase I

Comments: On January 7, 2007, Pharmasset announced the results of a trial in 50 HCV treatment naïve patients which found that R7128 (dosed twice daily) when used in combination with Pegasys and ribavirin was safe, well-tolerated and there were no serious adverse events reported in the 4-week treatment period. In the group that received 1500 mg 85% of the patients achieved undetectable HCV RNA.

Pharmasset announced preliminary results from a trial to evaluate a 1500 mg BID (twice a day) dose in combination with Pegasys and ribavirin in genotype 2 & 3 prior non-responders/relapsers and found that 90% were HCV RNA negative after 4 weeks of treatment.

Pharmasset also announced the preliminary results from a 31 patient study that found that the 1000 mg BID dose (in combination with Pegasys plus ribavirin) provided potent antiviral activity (88% HCV RNA negative) and the greatest margin of safety. Based on these results Pharmasset will advance the 1000 mg dose into larger trials.

AASLD 2008: HCV genotype 2 and 3 prior non-responders were treated with R7128 (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. R7128 was generally well-tolerated and further development in genotype 2 and 3 patients is being planned. *(November 7, 2008)*

SCH900518 (518)

Protease Inhibitor

[Schering](#)

Phase II

Comments: On November 24, 2008 Schering announced the results from a Phase I clinical trial of 518 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. *(November 28, 2008)*

VCH-759

Polymerase Inhibitor

[Virochem](#)

Phase II

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. *(November 19, 2007)*

**TMC435350
(TMC435)**

Protease Inhibitor

[Medivir/Tibotec](#)

Phase II

Comments: Following the successful completion of a phase I study with TMC435350 in both healthy volunteers and patients chronically infected with hepatitis C virus (HCV), Medivir announced a phase IIa study, TMC435350-C201, of the investigational hepatitis C (HCV) protease inhibitor TMC435350. The study will start shortly in Europe by Tibotec Pharmaceuticals Ltd., which is collaborating with Medivir on the development of TMC435350.

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).

AASLD 2008: A study found that the **Triple** combination of TMC435, pegylated interferon, plus ribavirin given for 28 days produced mean viral load reductions of 3.47 log₁₀ IU/mL in the 25 mg arm and 4.55 log₁₀ IU/ml in the 75 mg/day arm. *(November 7, 2008)*

**SCH 503034
(Boceprevir)**

Serine Protease
Inhibitor

[Schering](#)

Phase III

Comments: **AASLD 2008:** In the five arm study of boceprevir, the arm that included 103 patients achieved an SVR12 (twelve weeks post treatment) of 74% – 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 and taste changes in the boceprevir arms.

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. *(November 7, 2008)*

Telaprevir (VX 950)

Protease Inhibitor

[Vertex](#)

Phase III

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).

PROVE 3 interim data of 453 patients who did not achieve and sustained virological response (SVR) with a previous course of pegylated interferon plus ribavirin--non-responders by type of non-response were non-responders (41%), relapsers (73%), viral breakthroughs (44%).

Study 107: Interim results from another 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 (43%), partial responders (82%), relapsers (83%), and viral breakthroughs (0%). 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 93% of patients who received the q8h were HCV undetectable and 83-85 % who received the q12h dose were HCV undetectable. *(November 28, 2008)*

Drugs in Clinical Development (General)

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
ANA773	TLR Agonist	Anadys Pharmaceuticals	Phase I

Comments: Andays announced that they had begun dosing of ANA773 in people with chronic hepatitis C. The study will evaluate the safety and tolerability of ANA773 given to patients every other day for 28 days. Anadys expects to have viral load data from the 800-mg cohort in the first quarter of 2009 and additional data in the second quarter. *(November 5, 2008)*

CYT107	Immunomodulator	Cytheris	Phase I
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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. *(October 28, 2008)*

SPC3649 (LNA-antimiRTM-122)	microRNA	Santaris Pharma	Phase I
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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. *(May 29, 2008)*

CF102	A3AR AGONISTS	CAN-FITE	Phase I
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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. *(May 13, 2008)*

IMO-2125	TLR9 agonist	Idera Pharmaceuticals	Phase I
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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. *(September 18, 2007)*

PYN17	Botanical	Phynova	Phase I
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Comments: On September 12, 2007, Phynova announced completion of patient enrollment of 29 patients who will receive PYN17 or placebo. Results from the study found that it was well-tolerated with minor adverse events. Larger studies are being planned for 2008 *(December 13, 2007)*.

Bavituximab (formerly Tarvacin)	Anti-Phospholipid Therapy	Peregrine	Phase I
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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 $.5 \log^{10}$. Bavituximab was found to be generally safe and well-tolerated with no dose limiting toxicities or serious side effects reported. *(November 18, 2007)*

A-831	NS5A Inhibitor	Arrow Therapeutics Ltd	Phase I/II
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Comments: A832 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. *(December 12, 2007)*

NOV-205	Immunomodulator	Novelos Therapeutics	Phase I
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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)*

CTS-1027	Anti-inflammatory	Conatus	Phase II
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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. *(December 28, 2007)*

Oglufanide disodium	Immunomodulator	Implicit Bioscience	Phase II
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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
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Comments: **EASL 2008:** In a study of 96 treatment-naive and 24 treatment-experienced HCV genotype 4 patients in Egypt receiving triple therapy of nitazoxanide, pegylated interferon, and ribavirin, 79% achieved an SVR in the treatment-naïve group and 25% in the treatment-experienced group. In another study (STEALTH-C1) that used nitazoxanide monotherapy as a 4 to 12 week lead-in followed by the triple combination (pegylated interferon, ribavirin and mitazoxanide) it was found that the 4 week lead-in resulted in an overall 80% SVR12 (12 weeks post treatment). There were 44 patients in this study and the majority were HCV genotype 4 patients. Final results will be presented at AASLD 2008.

Currently there are 2 clinical trials using nitazoxanide in combination with pegasys and ribavirin in genotype 1 patients. **STEALTH C-2** will investigate the role of nitazoxanide (plus Pegasys/ribavirin) in 64 genotype 1 prior non-responders to peginterferon/ribavirin therapy. **STEALTH C-3** will investigate nitazoxanide (plus Pegasys/ribavirin) in 112 HCV genotype 1

treatment-naïve patients. Romark announced on May 21, 2008 that they have completed patient enrollment. STEALTH C-2/C-3 preliminary data is expected to be released in early 2009.

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. *(November 7, 2008)*

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. *(April 29, 2008)*

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-03491390 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)*

Civacir	HCV Immune Globulin	NABI	Phase II
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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. *(November 22, 2007).*

MX-3253 (celgosivir)	Glucosidase I Inhibitor	MIGENIX	Phase II
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Comments: **DDW:** Results from a phase II study of 57 (prior non-responder) patients in 3 treatment combination arms (celgosivir 400 mg/day plus peg-interferon and ribavirin, celgosivir 400 mg plus peg-interferon alone or placebo plus peg-interferon) were released which showed that triple therapy produced a substantial decrease in HCV RNA (viral load) compared to peg-interferon plus ribavirin (1.2 log₁₀ vs. 0.4 log₁₀).

On June 27, 2007 Migenix announced that Schering Plough Corporation would not enter into a period of exclusivity to negotiate terms of a license agreement for celgosivir.

In December 2007 Migenix announced the interim results of a study of 10 patients who completed 4-weeks of treatment, and celgosivir was found to be safe and well-tolerated when combined with pegylated interferon plus ribavirin. The study is a 20-patient, 12-week study and results are expected in early 2008.

On February 1, 2008 Migenix announced an additional dose of 600 mg (daily) to the study to test for safety and tolerability. *(February 10, 2008)*

VGX-410C (Mifepristone)	IRES Inhibitor	VGX Pharmaceuticals	Phase II
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Comments: VGX announced on September 2, 2007 that patient enrollment in their multi-site, multi-dose, and double-blind study has been completed. Patients will be treated for 28 days with a 28 day follow-up period. *(September 4, 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 (PEG-Interferon Lambda)	Long acting Interferon	ZymoGenetics	Phase I
Comments: <i>AASLD 2008:</i> In a small study of 6 HCV genotype 1 patients who were given IL-29 it was found that all of the patients had a 2 log or greater decrease in HCV RNA with 4 of the patients having less than 1000 HCV RNA copies at the end of treatment. IL-29 was found to be safe and well-tolerated. <i>(November 7, 2008).</i>			
Oral Interferon alpha	Oral Interferon	Amarillo Biosciences	Phase I
Comments: Testing low dose oral administration of alpha interferon absorbed through mucosal membranes. Phase II studies are being planned in cooperation with CytoPharm for the end of 2007. <i>(September 5, 2007)</i>			
Belerofon (oral)	Oral interferon	Nautilus Biotech	Phase II
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. <i>(May 29, 2007)</i>			
BLX-883 (Locteron)	Long Acting Interferon	Biolex Therapeutics / OctoPlus	Phase II
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).			
<i>EASL 2008:</i> Results from a Phase 2a, twelve-week study of 32 treatment-naïve HCV genotype 1 patients treated with Locteron (dosed once every two weeks) and ribavirin was released at EASL. In this study, the percentage of patients who achieved an early virological response (at least a two-log drop) was 100% (640 & 480 dose groups), 88% (320 dose group) and 37.5% (160 dose group). Locteron was generally well-tolerated with no serious adverse events except one patient in the 640 dose group had an inflammation of the ear which was resolved after treatment was stopped. <i>(April 29, 2008)</i>			
Omega Interferon	Interferon	Intarcia Therapeutics	Phase II
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.			
<i>EASL 2007:</i> 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	Long Acting Interferon (injections every two weeks)	Human Genome Sciences	Phase III
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Comments: On August 28, 2007, HGS announced that the enrollment in the first of the two phase III studies has been completed—ahead of schedule.

AASLD 2007: SVR rates for a phase II study of 458 HCV genotype 1 treatment-naïve patients was 58.5 and 55.5 % for patients treated with Albuferon (plus ribavirin) once every two weeks, 50.9% in the Albuferon (plus ribavirin) once every 4 weeks, and 57.9% for the Pegasys (plus ribavirin) group. Another study of 115 prior interferon treatment non-responders treated with various doses of Albuferon plus ribavirin for 48 or 72 weeks resulted in a overall SVR rate of 17.4%.

On January 23, 2008 Human Genome Sciences (HGS) announced that, based on the assessment of an independent Data Monitor Committee (DMC), the 1,200-mcg dosing arm of Albuferon is being discontinued due to serious pulmonary (lung) adverse events. The patients in the 1200-mcg will be rolled over to the 900 mcg dosing arm. The company stated that the DMC did not express any safety concerns about the 900-mcg dose of Albuferon. The company also stated that they did not expect the safety concerns would hold up the clinical trial process and they believe that HGS will be able to file for FDA marketing approval in 2009 with a possible 2010 approval date. *(January 29, 2008)*

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 9mcg and 15mcg doses of daily Infergen in combination with ribavirin in non-responders.

In December 2006, Valeant announced the initiation of a phase IV study to treat prior pegylated interferon/ribavirin non-responsive patients. 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.

On December 20, 2007, it was announced that Valeant sold Infergen to Three Rivers Pharmaceuticals. *(December 28, 2007)*

Vaccines in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
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ChronVac-C	DNA-based Therapeutic Vaccine	Inovio / Tripep	Phase I
<p>Comments: Tripep AB of Sweden has received approval from the Swedish Medical Products Agency to initiate a phase I/II clinical trial. Twelve HCV positive patients will be enrolled to study the safety, immune boosting and antiviral properties of this therapeutic vaccine. On November 27, 2007 Inovio announced that it had started the treatment of ChonVac-C to the first patient enrolled in their trial. Preliminary results from the first 5 patients treated showed no safety issues. On November 17, 2008 Inovio released data showing that in the highest dose group 2 of three patients demonstrated viral load reductions of 93% and 99.7%. while no reductions were seen in the lowest dose group. <i>(November 28, 2008)</i></p>			
TG4040	Therapeutic Vaccine	Transgene	Phase I
<p>Comments: On Oct 01, 2007 Transgene announced that the first patient of an expected 24 HCV-positive patients was enrolled in a study being conducted in Canada.</p> <p>On February 13, 2007, Transgene announced that it had begun enrollment in France of chronic HCV patients and that it will enroll a total of 15 patients to study the safety, tolerability, virological and immunological response of TG4040.</p> <p>Preliminary data was reported on May 19, 2008, and it was found that the drug was safe and well-tolerated and that six out of 15 patients experienced a viral load reduction ranging from .05 to 1.4 log₁₀. <i>(May 21, 2008)</i></p>			
PeviPROTM	Therapeutic vaccine	Pevion Biotect	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>AASLD 2007: A Phase 1b double-blinded, placebo controlled, dose-escalating, multi-center trial evaluating the safety, immunogenicity, and efficacy of GI-5005 found that 11% of patients receiving GI-5005 had viral load reductions from -0.75 to 1.4 log₁₀ and that dose response for ALT normalization reached 50% in the group receiving the highest dose (40 YU). GI-5005 was well tolerated with no dose limiting toxicities. A Phase 2b trial is being initiated comparing the triple therapy of GI5005, pegylated interferon, and ribavirin to the dual therapy of pegylated interferon and ribavirin.</p> <p>On December 19, 2007, GlobeImmune announced the initiation of a phase II study expected to enrol 120 patients who will receive Tarmogen in combination with pegylated interferon plus</p>			

ribavirin and compare the triple to regular standard of care (peg with ribavirin).

AASLD 2008: A study from GlobeImmune on their HCV therapeutic Vaccine, GI-5005, given to HCV patients with a high HCV viral load (>600,000 IU/mL) found that it doubled the clearance of HCV RNA. There were 140 HCV genotype 1 patients – 74% treatment naïve; 26% prior treatment non-responders in the 4 week trial. *(November 7, 2008)*

IC41	Therapeutic Vaccine	Intercell	Phase II
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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).

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).

Data released in December 2006 found a good safety profile of IC41 when used in combination with pegylated interferon and ribavirin. The study did not find a statistical improvement in relapse rate of the patients given IC41, but according to Intercell the doses were sub-optimal. An ongoing proof of concept study to assess the effectiveness of IC41 at an optimal dose is currently underway. The interim data from the first 25 patients found that there were statistically significant viral load reductions and a very good safety profile. The full study results from 50 patients are expected in the first quarter of 2008.

On February 7, 2008 Intercell announced that interim results found that in 50 patient treated with IC41 there was an average of 60% viral load reductions. *(February 10, 2008)*

Anti Liver Cancer Drugs in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
ZIO-101	Anti-Liver Cancer (Arsenic)	ZIOPHARM Oncology	Phase II

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.** *(May 29, 2007)*

GV1001 (Heptovax)	Anti-Liver Cancer	Pharmexa	Phase II
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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)*

PI-88	Anti-liver cancer	Progen Industries	Phase II
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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)*

Nexavar (sorafenib)	Anti-liver cancer	Onyx Pharmaceuticals	Phase IV
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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. *(September 12, 2008)*

ThermoDox (doxorubicin)	Anti-liver cancer	Celsion	Phase III
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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. The company also announced a new phase III trial of Doxorubicin in patients with hepatocellular carcinoma (HEAT study). *(July 3, 2008)*

Adjunct Therapies

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

Eltrombopag (Promacta)	Thrombopoietin Receptor Agonist	GlaxcoSmithKline	Phase II
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Comments: A recent study found that eltrombopag boosted platelet counts in a majority of patients at each of three dosage levels and the patients were able to continue or start HCV treatment.

On December 20, 2007, GSK announced that they had applied for FDA approval to market eltrombopag for short term treatment of chronic idiopathic thrombocytopenic purpura (ITP) (*December 28, 2007*)

Clinical trials on Hold

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
JBK-122	Anti-inflammatory	Jenken Biosciences	Phase II

Comments: The FDA approved JBK-122 for Phase II clinical studies. The drug jumped into Phase II studies since the safety of JBK-122 had already been studied in humans. The goal of the study is to treat or prevent liver damage caused by HCV-related inflammation. (*December 16, 2006*)

Doxorubicin Transdrug	Anti-liver cancer	BioAlliance Pharma	Phase II/III
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Comments: Drug-loaded nanoparticles that are used for the delivery of drugs through intra-arterial, intravenous, or oral administration to treat or slow down progression of primary liver cancer. Initiation of phase II studies has been approved in France. The phase II study will enroll 50 patients over three months. A larger Phase III trial is also being planned that will expand the trial to include up to 200 patients treated for 12 months. The Phase II and III study will evaluate disease progression to assess progression of liver cancer. Doxorubicin Transdrug has been granted orphan drug status by the EMEA (Europe) and FDA (United States). (*December 16, 2006*)

Although there was shown to be a clinical benefit, there were also more frequent and more severe pulmonary adverse events than expected. Based on this the trial has been suspended. (*July 16, 2006*)

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	<i>Studies Cancelled</i>

		Pharmaceuticals Int'l	
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 Inhibitor	ViroPharma/Wyeth	<i>Studies Cancelled</i>
HCV-AB68	Monoclonal antibody	XTL Bio	<i>Studies Cancelled</i>
XTL-6865 (formerly HepX-C)	Monoclonal Antibody	XTL Bio	<i>Studies Cancelled</i>
Suvus (Mehylene 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>

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