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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.
- 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.clincialtrials.gov.

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	NM-283
Bavituximab (Tarvacin)	Civacir	Albuferon		XTL-6865 (formerly HepX-C)
IL-29 (PEG-Interferon lambda)	Omega Interferon	ZADAXIN® (thymalfasin or thymosin alpha 1)		HCV-796
Medusa Interferon	Multiferon	Nexavar		
NOV-205	PF-03491390 (formerly IDN-6556)	Doxorubicin		
ITMN-191	IC41			
R1656	VX 950 (telaprevir)			
Belerofon (oral and injectable)	MX-3253 (Celgosivir)			
R7128	SCH 503034 (boceprevir)			
A-831	VGX-410C			
Oglufanide disodium	R1626			
PeviPROTM	DEBIO-025			
PYN17	GV1001			
TG4040	JBK-122			
AB68	PI-88			

ChronVac-R	BLX-883 (Locteron)			
GSK625433	MitoQ			
IMO-2125	SOV-07			
LGD-4665	Hepaconda			
	Alinia (nitazoxanide)			
	Suvus			
	Z10-101			
	VCH-759			
	Oglufanide disodium			
	TMC435350			
	GI-5005 (Tarmogen)			
	CTS-1027			
	Eltrombopag			

Table of Hepatitis C Drugs in Current Clinical Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
IMO-2125	**TLR9 agonist**	Idera Pharmaceuticals	Phase I
Comments: On September 17, 2007 Idera Pharmaceuticals announced that it started enrollment of patients to study the safety, tolerability and antiviral properties in prior null responder HCV patients. *(September 18, 2007)*			
AB68	Monoclonal antibody	XTL bio	Phase I
Comments: Results from single dose (15 patients) and escalating dose (25 patients) phase I trial found that AB68 was safe and well-tolerated with no serious adverse events. In addition, HCV-AB68 also showed significant reductions in HCV viral load. *(March 6, 2007)*			
PYN17	Botanical	Phynova	Phase I
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
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 daily 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 Therapuetics Ltd	Phase I/II
Comments: 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 Therapuetics, Ltd. There has been no further news about the development of A-831. *(December 12, 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)			
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 enrol 100 HCV patients for 4 weeks in a proof of concept trial. *(December 28, 2007)*			
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	www.romark.com	Phase II
Comments: AASLD 2007: In a study of 96 treatment naive and 24 treatment experienced HCV genotype 4 patients in Eygpt receiving triple therapy of nitazoxanide, pegylated interferon, and ribavirin, 79% achieved an SVR 12 weeks post treatment. Future studies are being planned in HCV genotype 1 patients. *December 14, 2007)*			
SCV-07	Broad spectrum immune stimulator	SciClone	Phase II
Comments: A randomized, placebo-controlled trial of 30 patients (prior treatment genotype 1 relapsers) has been initiated using SCV-07 (injectable) for 7 days to assess the antiviral properties. *(June 29, 2007)*			
MitoQ (mitoquinone)	Inflammation/ Fibrosis Inhibitor	Antipodean Pharmaceuticals	Phase II
Comments: A Phase II study will recruit 36 patients to study the effect of MitoQ on liver enzyme levels. *(February 9, 2007)*			

DEBIO-025	Cyclophilin inhibitor	DEBIO	Phase II
Comments: AASLD 2006: In a phase I study (15 days) of 23 HIV/HCV coinfected patients found that there was HIV and HCV antiviral activity in the dose administered. The clinical profile is promising, but there were 10 patients who developed hyperbilirubinaemia and 3 patients had decreases in platelets (but no bleeding episodes). Bilibrubin levels returned to normal after cessation of therapy. DEBIO has stated that further studies are needed on the adverse events. EASL 2007: Per a company press release in April 2007, Debio has finalized the first two cohorts of the phase II study in HCV treatment-naïve HCV patients and has initiated a trial using the highest dose combination of DEBIO-026 plus pegylated interferon. *(November 20, 2007)*			
PF-03491390 **(Formerly IDN-6556)**	Pancaspase Inhibitor	Pfizer Pharmaceuticals	Phase II
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)*			
Civacir	HCV Immune Globulin	NABI	Phase II
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. 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).*			
Suvus (Mehylene blue) formerly BIVN-401 (Virostat)	Antiviral	Bioenvision	Phase II
Comments: In September, 2006 Bioenvision, INC reported that in patients who received 50 days or 100 days of Suvus reported viral load reductions of 83% and 92% respectively. The drug was well tolerated – the only side effect reported in the press release was a slight discoloration of the feces. Larger studies are being planned. *(September 8, 2006)*			
MX-3253 (celgosivir)	Glucosidase I Inhibitor	MIGENIX	Phase II
Comments: DDW: 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 that found that triple therapy produced a substantial decrease in HCV RNA (viral load) compared to peg-interferon plus ribavirin (1.2 log ^{10} vs. 0.4 log ^{10}). 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. (December 13, 2007)			
VGX-410C (Mifepristone)	IRES Inhibitor	VGX Pharmaceuticals	Phase II

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)*

JBK-122	Anti-inflamatory	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)*

Hepaconda	Bezafibrate	Giaconda	Phase IIa

Comments: A phase II study has begun on genotype 1 prior non-responders to pegylated interferon plus ribavirin therapy. The study will evaluate benzafibrate with chenodeoxycholic acid for safety and efficacy. According to a company spokesperson the trial results are expected mid year 2008. (*November 20, 2007)*

Viramidine **(Taribavirin)**	Nucleoside Analogue	Valeant Pharmaceuticals Int'l	Phase IIb

Comments: A prodrug of ribavirin that specially targets the liver. In the VISER1 – Peg-Intron plus (Viramidine (600 mg) or ribavirin (weight based) – and VISER2 – Pegasys plus (Viramidine (600 mg/day) or ribavirin (weight based) – studies it was found that Viramidine achieved the safety endpoint with considerably lower rates of anemia, but that Viramidine did not meet the non-inferiority efficacy goal. Based on the retrospective data of drug exposure of Viramidine in the VISER1 and VISER2 trials, Valeant announced a new phase 2b study comparing higher doses of Viramidine in combination with Peg-Intron. There will also be a control group that will receive Peg-Intron plus ribavirin.

VISER 1 and VISER 2: Safety and Efficacy (Intent-to-Treat Analysis)

	Anemia (Hgb < 10g/dL		Sustained Virologic Response*	
Study	Viramidine	Ribavirin	Viramidine	Ribavirin
VISER 1 (N=970)	5%	24%	38%	52%
VISER 2 (N=962)	6%	22%	40%	55%

**Percent of Patients with Undetectable HCV RNA; NGI SuperQuant Assay, sensitivity to 39 IU/mL (100 copies/mL)*

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 plus 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. (April 5, 2007)

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 enrol 100 HCV patients for 4 weeks in a proof of concept trial. *(December 28, 2007)*

ZADAXIN® (thymalfasin or thymosin alpha 1)	Immunomodulator	SciClone/Sigma-Tau	Phase III

Comments: Boosts the immune system. Used in combination with interferon and ribavirin. The data from Phase III clinical trials in the U.S. with over 1,000 patients receiving Zadaxin in combination with pegylated interferon was released in December 2005. Data from this first study of patients without cirrhosis showed only modest improvement in SVR, but was not statistically significant. Data from the second clinical trial of (thymosin, pegylated interferon and ribavirin) in May 2006, showed that the "addition of SciClone Pharmaceuticals' Zadaxin to pegylated interferon alpha treatment in hepatitis C patients has failed to produce a significant benefit over pegylated

interferon alone." On December 28, 2006 SciClone and its European partner Sigma-Tau announced that full patient enrollment is complete for its phase 3 clinical trial evaluating the use of ZADAXIN® in combination with pegylated interferon alpha and ribavirin to treat patients infected with the hepatitis C virus. This trial is being conducted by Sigma-Tau in Europe and has enrolled a total of 553 patients. "We believe that ZADAXIN could increase the therapeutic efficacy of standard HCV treatment without additional side effects, particularly for non-responder HCV patients infected with a high viral load of the genotype 1 strain of the virus," Data from this trial are expected to be publicly announced by year-end 2008. *(December 28, 2006)*

Interferons in development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
IL-29 (PEG-Interferon Lambda)	Long acting Interferon	ZymoGenetics	Phase I
Comments: A phase 1 clinical trial of 20 healthy adults (17 received drug, 3 received placebo) who received one dose of IL-29 has been completed and it was found that the drug was safe and well-tolerated. A larger study in people with HCV (prior treatment relapsers) is being planned. *(December 13, 2007)*			
Belerofon (injectable)	Interferon (long-acting)	Nautilus Biotech	Phase I
Comments: A Phase I trial of this protease resistant long-acting form (injection once a week) of interferon will begin recruiting patients in Austin, Tx. The phase I study will evaluate the safety, tolerability and pharmacokinetics in healthy volunteers and compare the pharmacodynamics with Intron A and Pegasys. *(April 5, 2007)*			
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. *(September 5, 2007)*			
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. *(May 29, 2007)*			
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 Peg-Intron). A phase I study of 27 healthy volunteers was reported at EASL and found Locteron demonstrated that it was safe and well-tolerated. Octoplus announced a 12 week phase II clinical trial (SELECT 1– Safety and Efficacy of Locteron: European Clincial Trial 1) in a total 32 treatment-naïve genotype 1 patients. On July 27, 2007, results from SELECT 1 of the 160, 320, & 480 microgram dosing in combination with ribavirin found a favorable safety and tolerability profile. In addition it was reported that 100% of the patients achieved an early virologic response. Data from the 640 microgram dosing arm was released on October 12, 2007 and found that 100% of patients in that arm achieved an early virological response. *Commencement of a phase IIb clinical trial is expected to begin in the first half of 2008.* *(October 23, 2007)*			
Omega Interferon	Interferon	Intarcia Therapeutics	Phase II
Comments: Uses an implantable infusion pump that releases a steady amount of Omega 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:* Final results from this study found that 36% of patients who received daily Omega interferon plus ribavirin achieved SVR compared to 6% who received Omega interferon monotherapy. The company may study higher doses of Omega interferon. *(April 17, 2007)*			
Multiferon	Long Acting Interferon	Viragen	Phase II
Comments: A type of natural interferon that has been approved to treat HCV in various countries outside of the			

United States. No new clinical trials of multiferon have been announced in the U.S. *(September 5, 2007)*			
Albuferon	Long Acting Interferon	Human Genome Sciences	Phase III
Comments: On August 28, 2007, HGS announced that the enrolment in the first of the two phase III studies has been completed—ahead of schedule. The second phase III study is expected to complete enrolment by the end of 2007 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%. *(November 19, 2007)*			
Consensus interferon (Infergen)	Interferon	Three Rivers Pharmaceuticals	Phase IV
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
ChronVac-C	DNA-based Therapeutic Vaccine	INOVIO/Tripep	Phase I
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. *(December 1, 1007)*			
TG4040	Therapeutic Vaccine	Transgene	Phase I
Comments: On 2/13/2007 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. Interim results are expected by the end of 2007. 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. *(October 23, 2007)*			
PeviPROTM	Therapeutic vaccine	Pevion Biotect	Phase I
Comments: On December 18, 2006, Pevion Biotect 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. *(September 4, 2007)*			
HCV/MF59	Vaccine(s)	Chiron/Norvartis	Phase I
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 who received 4 different doses of vaccine produced HCV antibodies in all of the patients. The study is on-going.			
GI-5005 (Tarmogen)	Therapeutic Vaccine	Globe Immune	Phase II
Comments: A form of therapeutic vaccine that is believed to stimulate the immune system to help fight HCV. **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 log 10 and dose response for ALT normalization reaching 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.

On December 19th, GlobeImmune announced the initiation of a phase II study expected to enrol 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). *(December 28, 2007)*

IC41	Therapeutic Vaccine	Intercell	Phase II

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.

A larger trial is being planned in HCV genotype 1 patients who have never been treated to assess the decline in HCV RNA (viral load). *(September 04, 2007)*

Polymerase/Protease Inhibitors in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
GS9190	Polymerase Inhibitor	Gilead	Phase I

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 GS9190 was generally well-tolerated and showed antiviral activity against HCV. However, 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 the result of GS9190. If this problem can be resolved, Gilead will advance GS9190 into larger studies. *(November 18, 2007)*

GSK625433	Polymerase Inhibitor	GlaxcoSmithKline	Phase I

Comments: Currently recruiting patients to study the initial safety and tolerability in healthy adults as well as anti-viral activity. *(September 04, 2007)*

ITMN-191 (R-7227)	Protease Inhibitor	InterMune/Roche	Phase I

Comments: Results from the Phase Ia study found that ITMN-191 was safe and well-tolerated with no serious adverse events in 64 healthy subjects. On September 26, 2007 InterMune announced that it would start enrolment of the phase Ib clinical trial on about 40 HCV patients. The study will assess the viral kinetics, viral resistance, pharmacokinetics, safety and tolerability of ITMN-191 (two or three times a day; with and without food) for a period of 14 days. Future studies of ITMN-191 will include the combination of Pegasys and ribavirin. *(October 1, 2007)*

R7128	Polymerase Inhibitor	Pharmasset/Roche	Phase I
Comments: On January 7th, 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. *(January 12, 2007)*			
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)*			
R1626	Polymerase Inhibitor	Roche	Phase II
Comments: AASLD 2007: In a study of 104 patients, it was found that in the group with 30 patients who received R1626 (1500 mg bid) in combination with Pegasys and ribavirin, 81% were HCV RNA negative by week 4. In general the side effects were considered mild to moderate. However, there is concern because of the incidence of grade 4 neutropenia which was the major reason for dose reductions and treatment discontinuations. Roche has announced a new study of R1626 testing different doses of R1626 (500, 100, and 1500 mg bid) and Pegasys (90 ug and 180 ug) plus standard ribavirin dose to find the best dosing with the least side effects. *(November 18, 2007)*			
SCH 503034 (Boceprevir)	Serine Protease Inhibitor	Schering	Phase II
Comments: In two studies presented at AASLD 2005, 61 genotype-1 patients in a 14-day course of treatment (5 treatment arms including 1 placebo arm), showed an HCV RNA reduction with the maximum HCV reduction of more than 2 logs in the group receiving 400 mg of SCH503034. SCH503034 was safe and well-tolerated with no serious adverse events. In another study, SCH503034 in combination with Peg-Intron resulted in a decrease of more than 2 logs overall with 4 out of 10 subjects in the 400 mg arm achieving undetectable HCV RNA. Phase II studies with the combination of SCH503034 and Peg-Intron are underway. In April 2006, it was announced that patient enrollment in this trial was completed. In January 2006 the FDA granted Fast Track Designation. On October 18, 2007, Schering reported preliminary data that found that 79% of the patients who received 800 mg TID of boceprevir in combination with Peg-Intron plus ribavirin achieved an early virological response. *(October 23, 2007)*			
VX 950 (telaprevir)	Protease Inhibitor	Vertex	Phase II
Comments Vertex has initiated two large multi-international studies (Prove 2 and Prove 3) of Genotype 1, treatment naïve and treatment experienced patients. AASLD2007: Results from the phase II studies in the 24 week treatment arms: Dose: Telaprevir (pill) taken every 8 hours, pegylated interferon (Pegays) injected once a week, and weight-based ribavirin (pill, 1000/1200 mg/day). **PROVE 1:** 61% achieved a sustained virological response (SVR-24 week post treatment). **PROVE 2:** 65% achieved a response (interim results 12 weeks post treatment). Side effects that required treatment discontinuation were higher in the telaprevir triple arms compared to the pegylated interferon plus ribavirin arm (control arm) in both PROVE 1 and PROVE 2 (10-15%, vs. 2-5% respectively). **PROVE 3** (treatment of prior non-SVR responders) results are expected in 2008. Larger phase III studies are being planned for 2008. *(November 19, 2007)*			

TMC435350	Protease Inhibitor	Medivir/Tibotec	Phase II

Comments: Medivir announced that, following the successful completion of a phase I study in both healthy volunteers and patients chronically infected with hepatitis C virus (HCV), the 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., who are 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 SoC to allow evaluation of sustained virologic response (SVR). *(November 21, 2007)*

Anti Liver Cancer Drugs in Development

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
ZIO-101	Anti-Liver Cancer (Arsenic)	ZIOPHARM	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
Comments: Initiation of phase II studies has begun in France, Spain and Germany to treat liver cancer (HCC).The trail 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
Comments: A treatment for primary liver cancer following surgical resection of a liver tumour. 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% 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)*			
Doxorubicin Transdrug	Anti-liver cancer	BioAlliance Pharma	Phase II/III
Comments: Drug-loaded nanoparticles that are used for the delivery of drugs though intra-arterial, intravenous, or oral administration to treat or slow down progression of primary liver cancer. Initiation of phase II studies have been approved in France. The phase II study will enroll 50 patients over three months. A larger Phase III trial is also being planed that will expand the trial to include up to 200 patients treated for 12 months. The Phase II and III study will evaluate the disease progression to assess the disease progression of liver cancer. Doxorubicin Transdrug has been granted orphan drug status by the EMEA (Europe) and FDA (United States). *(December 16, 2006)*			

Nexavar (sorafenib)	Anti-liver cancer	Onyx Pharmaceuticals	Phase III- **FDA Approved**
Comments: It has been reported that in two clinical trials that that Nexavar significantly improved overall survival rates of patients with liver cancer and without any adverse events. Based on these data, the company has halted the clinical trial so that all the patients (including the placebo arm) in the trial could receive Nexavar. According to a company press release, Onyx plans to seek approval from the FDA and European health authorities as soon as possible. Bayer HealthCare Pharmaceuticals Inc. and Onyx Pharmaceuticals, Inc. announced on June 27, 2007 that a Supplemental New Drug Application (sNDA) for **Nexavar**(R) (sorafenib) tablets has been submitted to the U.S. Food and Drug Administration (FDA) for the treatment of patients with hepatocellular carcinoma (HCC), the most common form of liver cancer. The company announced on August 20, 2007 that the FDA has granted Nexavar priority review, which means that the review process is expediated and the FDA will take action within sex months of the date on which the FDA received the application. On November 19, 2007 Bayer AG announced that Nexavar had been approved by the FDA for the treatment of hepatocellular carcinoma (HCC), which is the most common form of liver cancer. *(November 21, 2007)*			

Adjunct Therapies

Drug Name	Drug Category	Pharmaceutical Company	Clinical Phase
LGD-4665	Thrombopoeitin Receptor Agonist	Ligand Pharmaceuticals Inc.	Phase I
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. *(December 28, 2007)*			
Eltrombopag (Promacta)	Thrombopoeitin Receptor Agonist	GlaxcoSmithKline	Phase II
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
XTL-6865 (formerly HepX-C)	Monclonal Antibody	XTL Biopharmaceuticals	Phase I
Comments: Results from a phase I trial evaluating XTL-6865 found that it was safe in the doses given. XTL Bio announced that it is seeking a collaborative partner for future development of the drug. A future clinical trial will evaluate this compound in patients with hepatitis C undergoing liver transplantation. XTL is considering selling the rights to XTL-6865 or pursuing clinicial trials with a partner. *(June 8, 2007)*			
HCV-796	Polymerase Inhibitor	ViroPharma/Wyeth	Phase II

Comments: Phase II studies began recruiting and are expected to complete enrollment in the second quarter of 2007. The Phase II study will evaluate the safety, tolerability, antiviral activity, and pharmacokinetics of HCV-796 in combination with pegylated interferon plus ribavirin vs. pegylated interferon plus ribavirin in HCV genotype 1 treatment naïve patients and in genotype 1 patients who were non-responders to a previous course of HCV treatment. Treatment duration will be 48 weeks with a 24 week follow-up period. 4 week data will be released in the 3rd quarter of 2007; 12-week data will be released in the 4th quarter of 2007.

EASL:
Phase 1b data (in combination with PEG_Intron) reported that there was an additive antiviral effect across multiple genotypes in treatment naïve patients. The HCV-796 twice daily dose used in combination with Peg-Intron was generally well-tolerated – side effects were consistent with the known side effects of interferons. There were no dose limiting toxicities reported.

On June 13, 2007, Viro Pharma reported that the enrolment in 500 mg arm of the trial has been completed. On June 27, 2007 ViroPharma announced that the FDA granted fast track designation to HCV-796.

Clinical Trial On-Hold: On August 10, 2007 ViroPharma announced that it is discontinuing the dosing of HCV-796 due to safety concerns. Viropharma will continue to monitor the study participants for safety issues and the effectiveness of the drug in patients treated. ViroPharma in collaboration with Wyeth will determine the next steps in the development of HCV-796 based on the review of safety and efficacy data. *(August 17, 2007)*

Clinical trials that have been cancelled:

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

	Antibody		
JTK 003	Polymerase Inhibitor	Akros Pharma	*Studies Cancelled*
ISIS 14803	Antisense	Isis Pharma	*Studies Cancelled*
CEPLENE	Histamine	EpiCept	*Studies Cancelled*
INTERFERON GAMMA-1B	Anti-fibrotic	InterMune	*Studies Cancelled*
ANA971	Isatoribine	ANADYS	*Studies Cancelled*
CPG 10101 (ACTILON)	Immunomodulator	Coley	*Studies Cancelled*
GS9132/ACH806	Protease Inhibitor	Gilead/Achillion	*Studies Cancelled*
XTL-2125	Polymerase Inhibitor	XTL Biopharmaceuticals	*Studies Cancelled*
ANA 975	Isatoribine	ANADYS	*Studies Cancelled*
AVI-4065	Antisense Compound	BioPharma	*Studies Cancelled*
UT-231B	Imino Sugar Inhibitor	United Therapeutics	*Studies Cancelled*
G1262570	Anti-fibrotic	GlaxoSmithKline	*Studies Cancelled*
EMZ702	Interferon Enhancer	Transition Therapeutics,	*Studies Cancelled*
INTERFERON BETA-1A (REBIF)	Interferon	Ares-Serono	*Studies Cancelled*
INNO0101 (E1)	Therapeutic Vaccine	Innongenetics	*Studies Cancelled*
AMANTADINE	Broad Antiviral	Endo Labs Solvay	*Studies Cancelled*
R7025 (MAXY-alpha)	Pegylated interferon	Maxygen/Roche	*Studies Cancelled*
NM283 (Valopicitabine)	Polymerase Inhibitor	Idenix Pharmaceuticals	*Studies Cancelled*

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