

YBPS Marketing Case Competition 2008

HCV-908: The Path Forward



Team 7

Kelly Fitzgerald, MD, PhD Candidate

Alex Marzuka, MD Candidate

Corey Probst, MBA, MPH Candidate

Stephanie Shuping Wang, PhD Candidate

Pauline Wyrembak, PhD Candidate

November 14, 2008

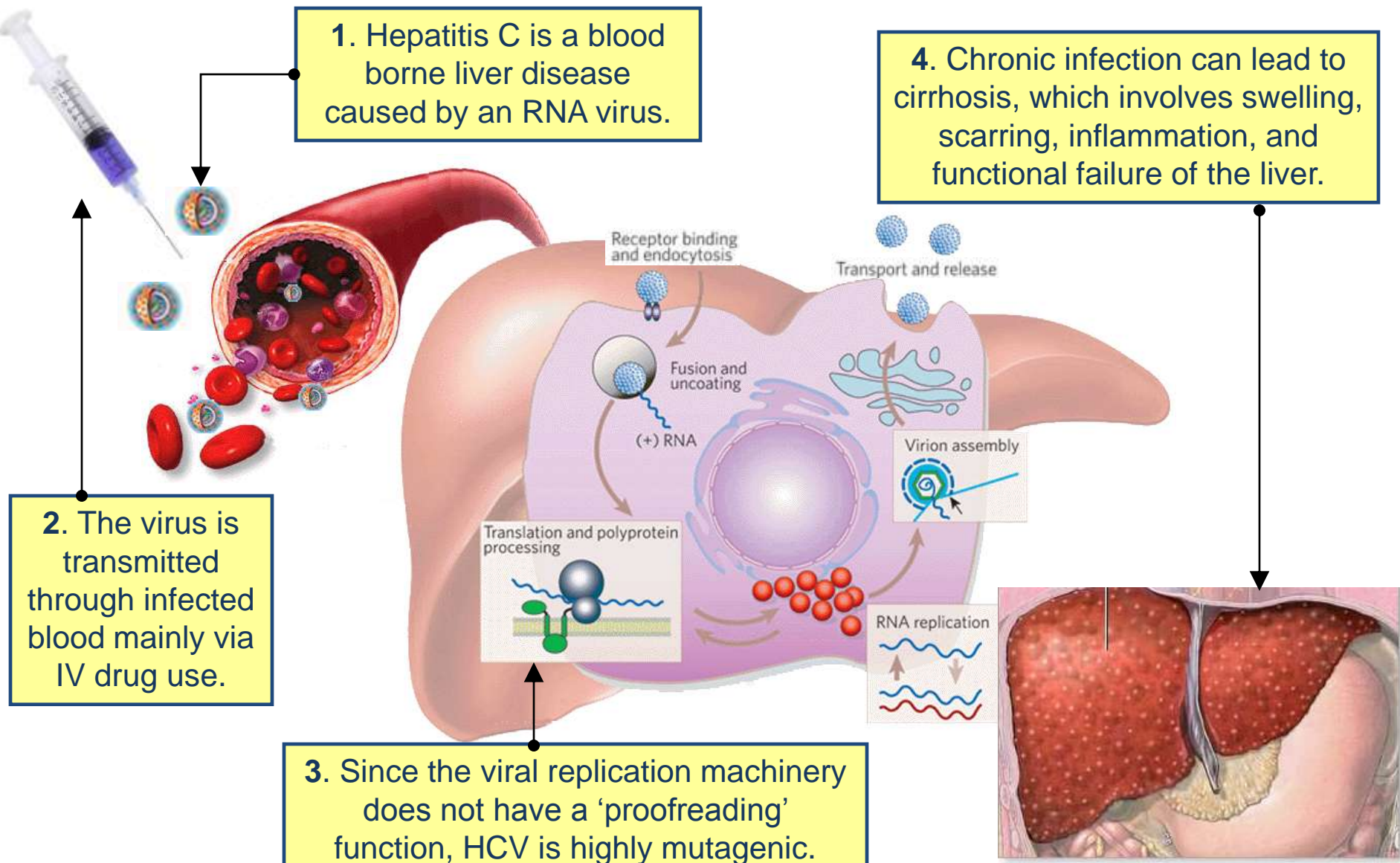
Hepatitis C

1. Hepatitis C is a blood borne liver disease caused by an RNA virus.

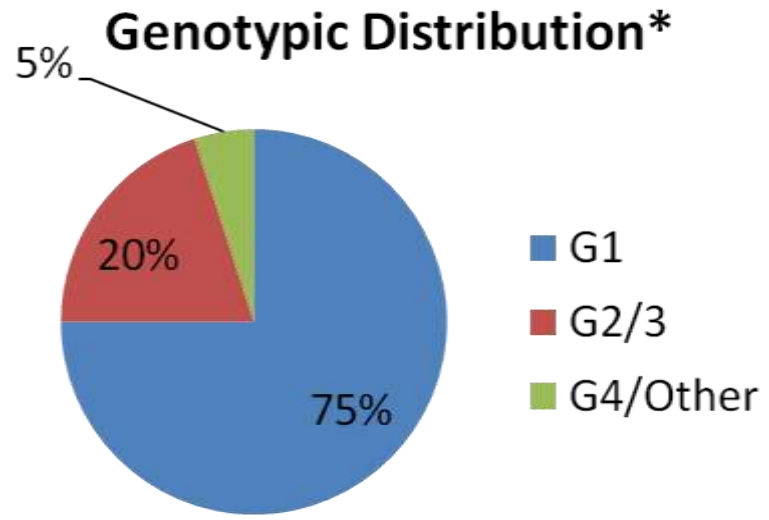
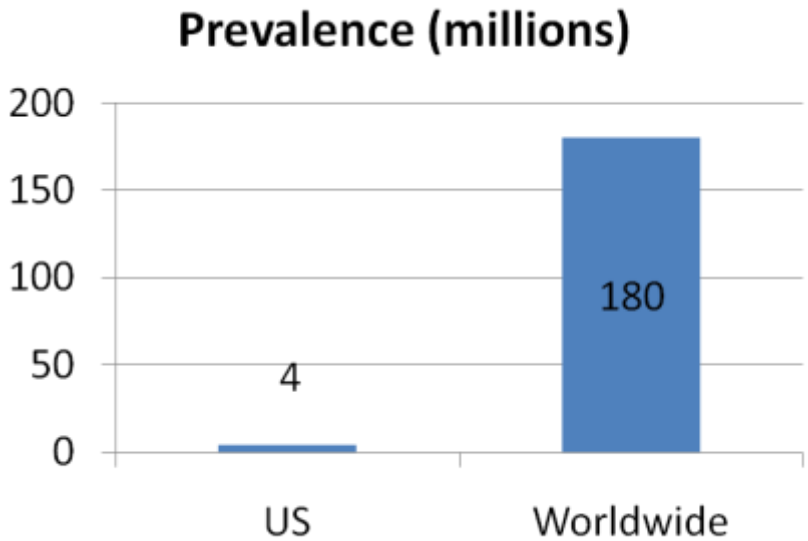
2. The virus is transmitted through infected blood mainly via IV drug use.

3. Since the viral replication machinery does not have a 'proofreading' function, HCV is highly mutagenic.

4. Chronic infection can lead to cirrhosis, which involves swelling, scarring, inflammation, and functional failure of the liver.



Epidemiology of HCV



• US Incidence: 35,000 cases /year

*Based on US distributions

*** Genotype 1 is the least responsive to current treatments**

Severe Sequelae	
Acute hepatitis	5 - 30%
Chronic Infections	4 - 24%
Chronic liver disease	> 2 - 12%

Current Treatment

- **Current SOC: once-weekly injections of pegylated interferon α (PEG-IFN α) and once-daily administration of Ribavirin for 24 to 48 weeks (for Genotypes 2/3 and 1, respectively)**
 - Only 50% of patients achieve a sustained viral response (SVR) of undetectable virus RNA levels 6 months after treatment cessation.
 - 25% of patients who initially respond to treatment relapse within six months.
 - **This leads to an overall treatment failure rate of ~63%.**
- **Serious side effects include anemia, neutropenia, thrombocytopenia, fatigue, and muscle weakness.**



Doctors hesitate to recommend treatment to mostly asymptomatic patients and patients are reluctant to undergo treatment.

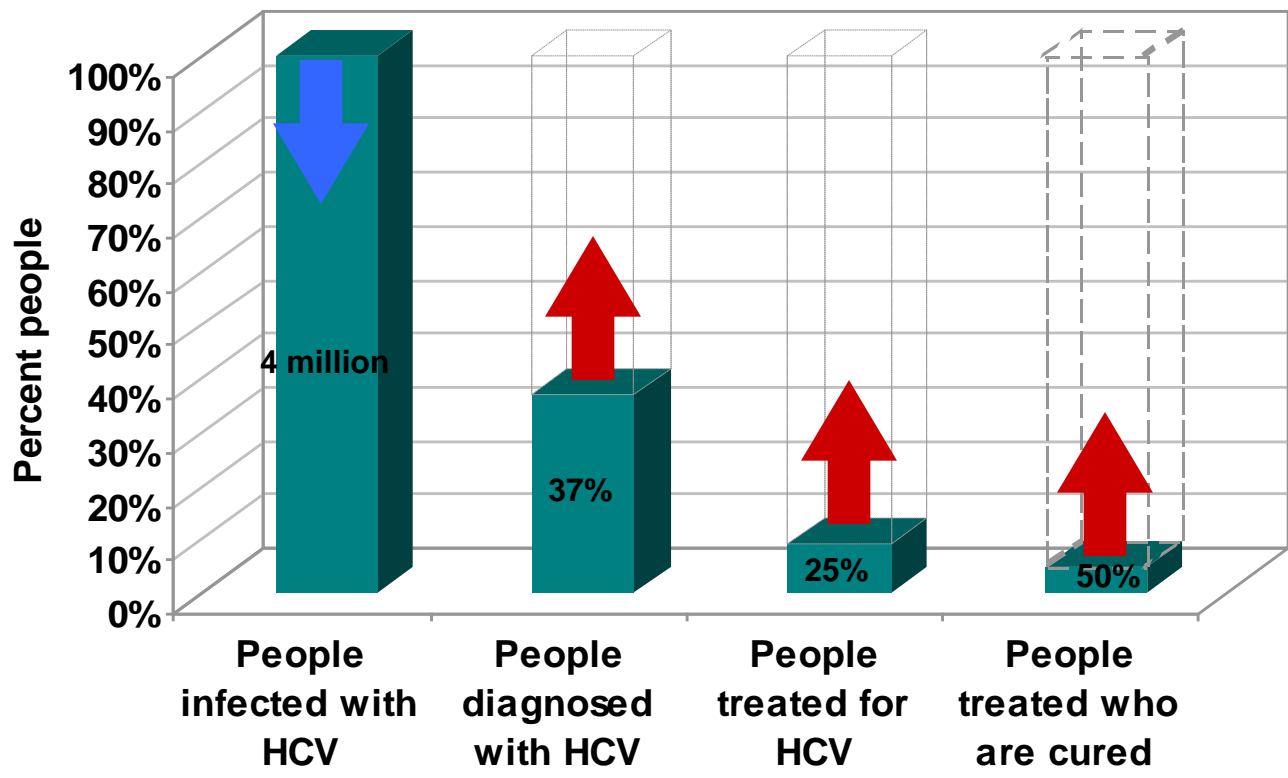

PEGASYS[®]
(Peginterferon alfa-2a)

COPEGUS[®]
(Ribavirin, USP) 200 MG TABLET


Pegintron
Peginterferon alfa-2b


Rebetol[®]
ribavirin

US Market Dynamics





Only 25% of patients diagnosed are treated, and of those only 50% respond to the current standard of care. Low diagnosis rates stem from the length of disease progression and the lack of symptoms at early stages. **Opportunity:** Next-generation drugs with different modes of action and/or efficacy will increase HCV detection, previous non-responders and new patients.

Source: Forbes <http://www.forbes.com/health/feeds/hscout/2007/05/21/hscout604788.htm>

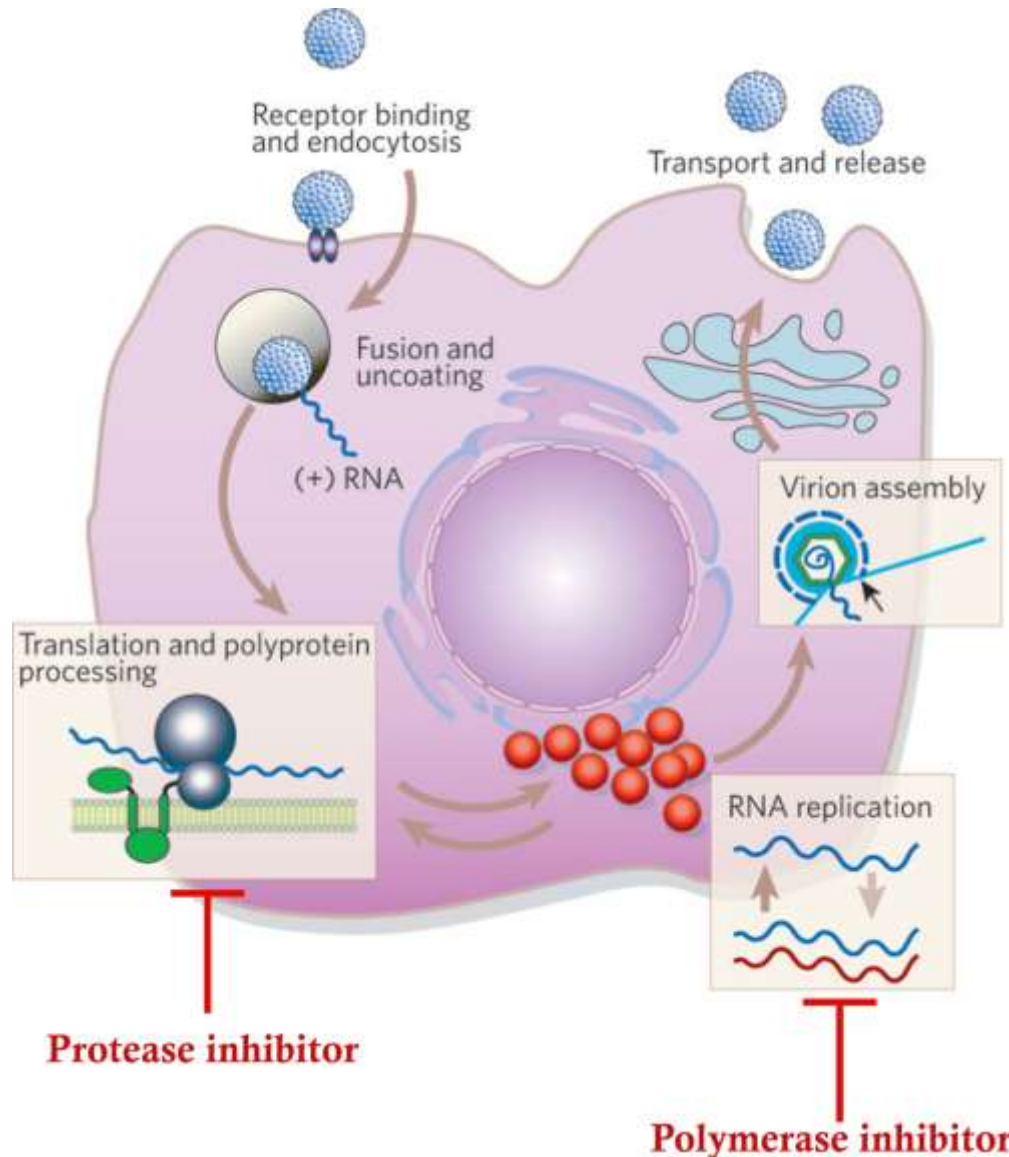
Competitive Landscape: Emerging Therapies

Several compounds are being studied.

Telaprevir and Boceprevir will likely be the first to market in 2011.

	Telaprevir	Boceprevir
	 <p>Oral, small molecule, protease inhibitor.</p>	 <p>Oral, small molecule, protease inhibitor.</p>
PROS	<ul style="list-style-type: none"> • Effective in Genotype 1. • 24 week treatment duration, cutting the current SOC in ½. • Promising results in non-responders, relapsers, partial responders. 	<ul style="list-style-type: none"> • Effective in Genotype 1. • Promising results in non-responders.
CONS	<ul style="list-style-type: none"> • Strict q8h dosing schedule. • Phase II trials show significantly more discontinuations due to rash compared to control. 	<ul style="list-style-type: none"> • Most likely a 48 week treatment duration. <p>•Sources: 1. Vertex press release to investors: http://investors.vrtx.com/releasedetail.cfm?ReleaseID=344629 2. Schering-Plough press release to investors: http://press.schering-plough.se/pressrum/pressarkiv/2008/boceprevir-phase-ii-study-showed-high-rate-of-sustained-response-with-28-and-48-week-regimens-in-genotype-1-treatment-naive-hepatitis-c-patients/</p>

HCV-908 Value Proposition



Different mechanism of action

- Agents with different mechanisms of action show limited cross-resistance.
- The future of HCV therapy will involve combination therapy with drugs that have different modes of action.

Pricing HCV-908

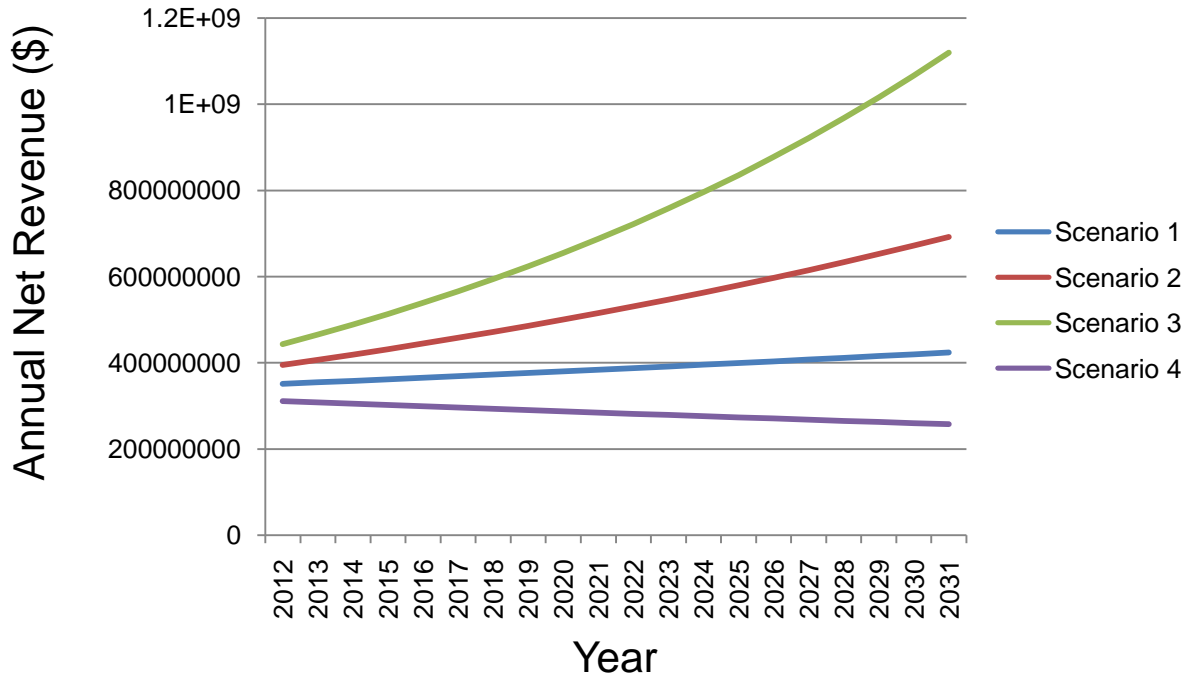
- Based on US HMO's current willingness to pay.
- Excess created for Genotype 1 by reducing current standard of care from 48 weeks to 24 weeks.

	Excess Willingness to Pay (48 weeks)	Excess Willingness to Pay (24 weeks)	Wholesale Price (24 weeks)
Genotype 1	\$3,593.61	\$14,681.42	\$11,745.14
Genotype 2/3	(\$10,318.48)	\$769.33	---

- Annual wholesale cost of treatment per patient (24 week regimen) = \$11,745.
 - Assumes a 25% retail price mark-up.
- Not cost-effective as first-line treatment for Genotype 2/3 patients.
- Pursue as 1st line treatment for Genotype 1 (largest revenue potential), and 2nd line treatment for other non-responders (nominal added value).

Valuing the US Market

Projected Annual Net Revenue from Total US HCV Market



Assumptions:

- 32% profit margins (excluding R&D).
- Phase III costs = \$333M
- Discount rate = 10%
- 20 year time period (beginning 2012).
- Based on US market share of treated Genotype 1 patients.

Scenario	Assumption	NPV	Market Share Needed
1	1% market growth	\$2,398,405,482.15	13.9%
2	3% market growth	\$3,099,633,430.43	10.7%
3	5% market growth	\$4,031,862,685.10	8.3%
4	-1% market growth	\$1,867,555,056.32	17.8%

Recommendation: Pursue Phase III Trials

Study treatment in largest possible market.

- Conduct trials in multiple populations.
 - Genotype 1: Treatment-naive patients, non-responders, and relapsers.
 - Genotypes 2 and 3: Non-responders and relapsers.

Remain competitive with other emerging therapies.

- RCTs of Peg-IFN + Ribavirin vs. HCV-908 + Peg-IFN + Ribavirin.
 - Consistent with Phase II trials, competitor trials.

Remain competitive against Telaprevir if 24 week trials are successful.

- Study treatment durations of 24 and 48 weeks.

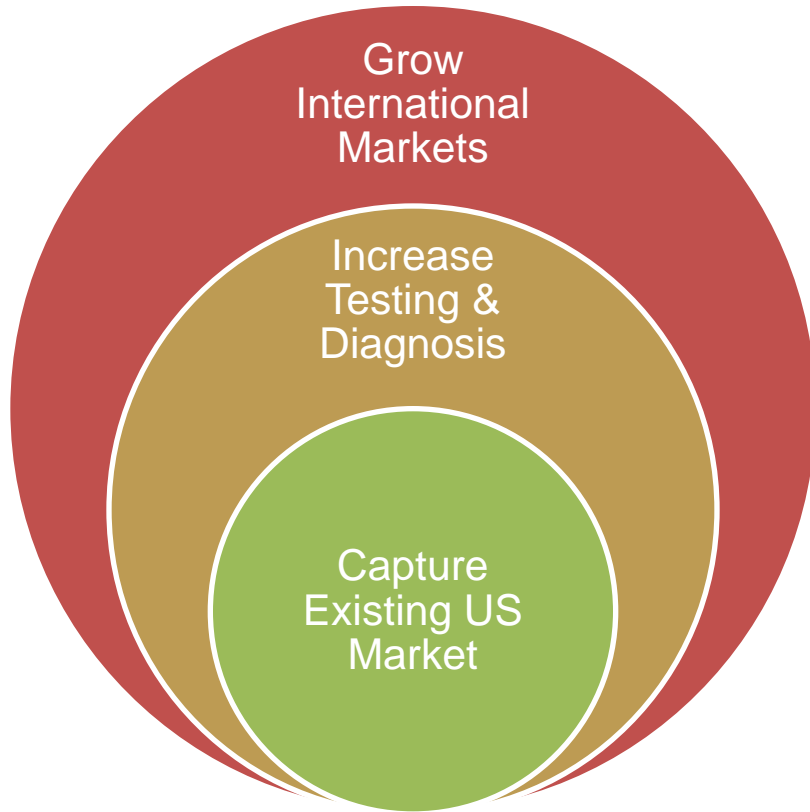
Opportunities for 2nd mover advantage

Reap benefits of efforts by Vertex and Schering-Plough to increase market size.
Learn from others' clinical trials experience.

- FDA expectations.
- Key benchmarks to remain competitive.

Claiming a Piece of the Pie

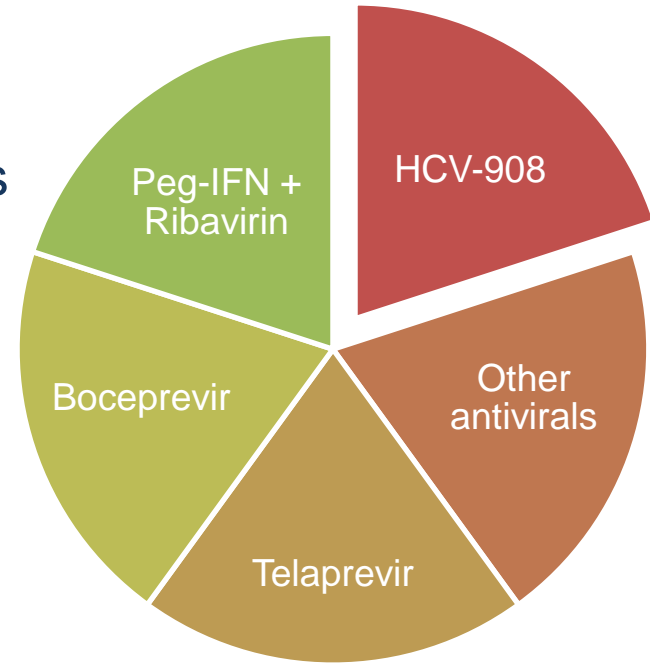
Market Growth



1. Cost effectiveness analyses
2. Quality of life studies
3. Diagnostic guidelines
4. Access to screening tests

Market Share

Players
Patients
Physicians
Payers



1. May be more resistant to mutations than competitor drugs
2. Potential for synergistic drug cocktail of polymerase inhibitors + protease inhibitors

Acknowledgements

Boehringer-Ingelheim

CRA

Easton Associates

McKinsey

Pfizer

Roche

Vion

Yale Biotechnology & Pharmaceutical Society

Yale School of Management

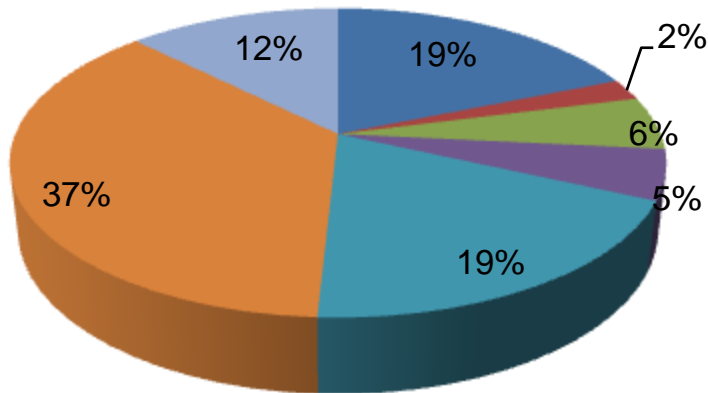
Yale School of Management Center for Customer Insight

Appendix

International Market: An Opportunity to Pursue?

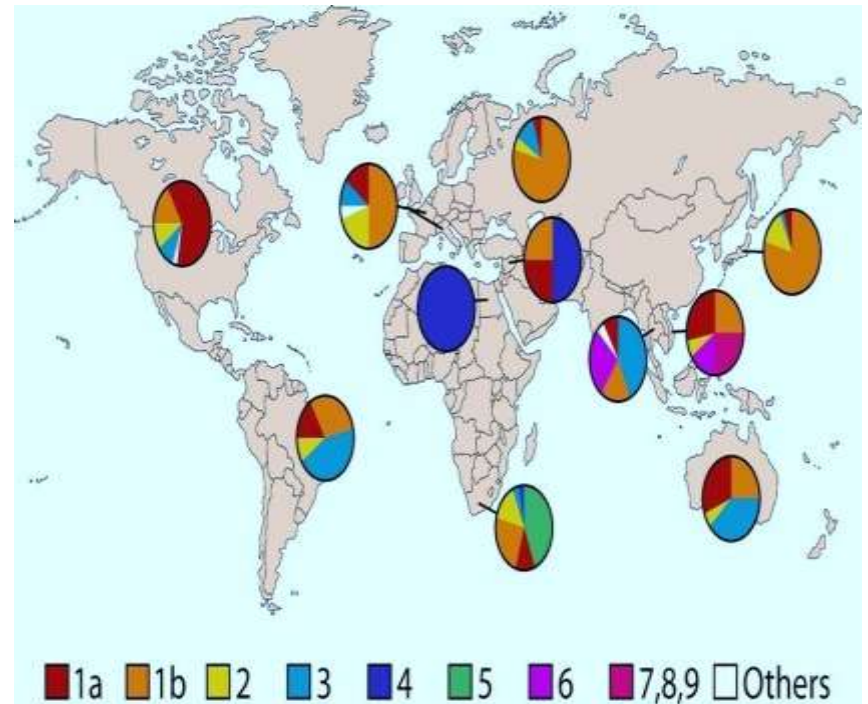
Worldwide Distribution of HCV Infected (N=180,000,000)

- Africa
- US
- N & S America (excluding US)
- Europe
- South-East Asia
- Western Pacific
- Eastern Mediterranean



World Health Organization

Worldwide Distributions of hepatitis C genotypes



Johns Hopkins Bloomberg School of Public Health

Other Drugs in Development

Group	Product name	Mechanism	Patient group	Phase	Advantage	Disadvantage
Polymerase inhibitors	HCV NS5B RNA (ViroChem Pharma)	non-nucleoside polymerase inhibitor	N/A	II		In 31-patient proof of concept study, 78% experienced diarrhea
	R-1626 (Roche)	polymerase inhibitor	treatment-naïve	II	High barrier to resistance; effective against all genotypes administered twice daily	Grade 4 neutropenia in several patients;
	HCV-796 (Wyeth)	non-nucleoside polymerase inhibitor	healthy, treatment naïve, non-responders	II (on hold)		8% of patients had elevated liver enzymes; ALT remained elevated in 50% after end of treatment
	Valopicitabine (Novartis)		polymerase inhibitor Non-responders, treatment-naïve	II (on hold);		discontinued permanently after FDA expressed concerns over safety
Others	KPE02003002 (Kemin Pharma)	non-nucleoside antiviral	Non-responders	II		No updates since 2004
	Viramidine (Schering)	prodrug with fewer side effects	treatment-naïve	II	prodrug of ribavirin is activated specifically in the liver, reducing systemic side effects	less efficacious than ribavirin (as shown in 2006 Phase III trial)