Evaluate Vantage

April 24, 2012

Hep C competitors need to make most of window of opportunity

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Gilead Science's valuation has grown by $3.6bn since a swathe of data released at the EASL conference last week confirmed the impressive potency of its hepatitis C agent, GS-7977. Now worth $39bn, the US drug developer previously best known for its HIV medicines has certainly found what is projected to be a worthwhile new calling.

Even before the liver conference equity analysts were pencilling in sales of $6bn by 2018 for the drug, consensus data from *EvaluatePharma* show, making GS-7977 the most valuable pipeline product in development across the industry. By comparison, forecasts for other hep C agents in development are relatively modest (see tables). The hepatitis C landscape has already been transformed by the first protease inhibitors, Incivek and Victrelis, whose days are remarkably already numbered; very swift shifts in the market are projected to continue. Competing companies will need to work hard to make the most of what could be narrow windows of opportunity.

Top five R&D drugs

Rank	Product	Company	Pharmacological Class	Indication	Status	2018 WW sales ($bn)	NPV ($bn)
1	GS-7977	Gilead Sciences	Hep C nucleoside NS5B polymerase inhibitor	Hepatitis C	Phase III	6.1	20.0
2	AMR101	Amarin	Omega-3 fatty acid	Hyperlipidaemia	Filed	3.3	8.3
3	Quad	Gilead Sciences	NRTI, HIV integrase inhibitor & CYP3A inhibitor	HIV	Filed	2.8	4.2
4	BG-12	Biogen Idec	Fumarate	MS	Filed	2.6	8.4
5	Pertuzumab	Roche	Anti-HER2 (ErbB-2) Mab	Breast cancer	Filed	2.4	8.5

Vertex's protease inhibitor might have set records for the fastest ever launch but it might also do the same for the fastest ever peak (*Incivek set to break record for fastest product launch, November 3, 2011*). After reaching the US and European markets in early 2011 and achieving global sales of $1.2bn that year, analysts reckon the arrival of newer classes of agents mean sales of the drug will peak in 2013, at $3.1bn.

Revenues are not seen dropping off a cliff – by 2018 global sales could still be close to $2bn, consensus data show – but the requirement to be used in conjunction with interferon and ribavirin mean all-oral combinations are viewed as the growth area.

What those combinations will look like is still uncertain, although it seems likely GS-7977 will among the first launches with estimates already reflecting huge potential (*EASL - Gilead's GS-7977 confirmed as lead oral hep C contender, April 19, 2012*).

Others in the pipeline with first-mover, all-oral potential should see upgrades in coming months. These include Bristol-Myers Squibb's hepatitis C portfolio, which has surprisingly low estimates attached given that the ability to combine agents is likely to be the key to developing a sustainable franchise in this space. Daclatisvir in particular is considered the most promising looking NS5A inhibitor in development, and has relatively minimal estimates at this stage.

Encouraging results from the Co-Pilot study run by Abbott with its protease inhibitor, ABT-450 and non-nucleoside polymerase inhibitor ABT-333 should see these agents get more attention.

Window of opportunity

Hepatitis C is a huge area of research right now and the table below provides only a snap shot of agents with sales forecasts attached or showing potential. The phase II and I pipeline is broad and growing, with many companies working towards grabbing a piece of the action.

The exact size of the hepatitis C market is not really known as many patients – some believe up to a third – are undiagnosed. Infections rates should be falling in developed nations, as better testing has eradicated accidental infections through blood transfusions. However, the market is considered large by any standards, clinically and commercially - around five million are believed to be infected with genotype 1 in the US, Europe and Japan, according to Mark Schoenebaum at ISI Group.

Despite this sizeable opportunity many believe the market could begin to shrink in 2016 and beyond in places like the US and Europe, as the easier-to-treat patients are cured (*EP Vantage interview - Idenix tries to play catch-up in torrid hep C race, April 24, 2012*). Which means to capitalise on the large pool of patients available in countries able to afford these new agents, competitors need to get to market fast. It is rarely the case that first-in-class is best-in-class, and the likes of GS-7977 and daclatisvir could well be bested in the future, and fade as fast as Incivek.

Long term view

The key to a sustainable franchise in this space will be the ability to treat patients with particularly resistant strains, or develop drugs that can be combined with other agents without increasing toxicity.

A belief that resistance will always be an issue for this disease, despite the emergence of incredibly effective treatments for some patients, means companies are still working in the very early stages of hepatitis C research. Astex Pharmaceuticals, for example, intends to put a novel class of direct acting agents into phase I trials later this year."

Resistance will always be a problem because of the rate hepatitis C replicates," said Neil Thompson, Astex's senior vice president of biology, speaking to *EP Vantage* at EASL. "A novel mode of action means the resistance profile is different from other compounds so will be valuable for future combinations. And this particular agent we've designed very carefully to be free from those drug-drug interaction problems."

For companies playing the longer-term game, they need to be looking beyond the common genotypes to patients with resistant subtypes and co-infections, such as HIV, Mr Thompson believes.

The short-term game looks already to have been won. Longer term, there is still much to play for.

Selected hepatitis C pipeline products

Status	Product	Generic name	Company	Pharmacological Class	Estimated launch	Annual Sales 2018 ($m)
Phase III	GS-7977	-	Gilead Sciences	Hepatitis C nucleoside NS5B polymerase inhibitor	30/09/2014	6,055
	TMC435	simeprevir	Johnson & Johnson/Medivir	Hepatitis C protease inhibitor	31/12/2013	797
	BMS-790052	daclatasvir	Bristol-Myers Squibb	Hepatitis C NS5A inhibitor	30/06/2014	422
	PEG-IFN-lambda	peginterferon lambda-1a	Bristol-Myers Squibb	Interferon lambda	30/06/2014	270
	DEB025	alisporivir	Novartis	Cyclophilin inhibitor	31/12/2014	108
	BMS-650032	asunaprevir	Bristol-Myers Squibb	Hepatitis C NS3 protease inhibitor	30/06/2015	90
	MK-7009	vaniprevir	Merck & Co	Hepatitis C protease inhibitor	31/12/2014	85
	BI 201335	-	Boehringer Ingelheim	Hepatitis C NS3/4A protease inhibitor	31/03/2013	-
Phase	IDX-184	-	Idenix	Hepatitis C polymerase	31/12/2015	393

II	IDX-184	-	Pharmaceuticals	inhibitor	31/12/2015	395
	INX-189	-	Bristol-Myers Squibb	Hepatitis C nucleotide NS5B polymerase inhibitor	31/12/2015	255
	RG7128	mericitabine	Roche	Hepatitis C nucleoside NS5B polymerase inhibitor	31/12/2016	113
	MK-5172	-	Merck & Co	Hepatitis C NS3/4A protease inhibitor	31/12/2015	-
	TG4040	hepatitis C vaccine	Transgene	Hepatitis C vaccine	31/12/2015	64
	Danoprevir	danoprevir	Roche	Hepatitis C protease inhibitor	30/06/2015	-
	VX-222	-	Vertex Pharmaceuticals	Hepatitis C non-nucleoside NS5B polymerase inhibitor	31/12/2015	-
	ABT-333	-	Abbott Laboratories	Hepatitis C non-nucleoside NS5B polymerase inhibitor	31/12/2015	34
	ABT-450	-	Abbott Laboratories	Hepatitis C protease inhibitor	31/12/2016	28
	ABT-072	-	Abbott Laboratories	Hepatitis C non-nucleoside NS5B polymerase inhibitor	31/12/2016	28
	BMS-791325	-	Bristol-Myers Squibb	Hepatitis C NS5A inhibitor	30/06/2016	23
	GS 5885	-	Gilead Sciences	Hepatitis C NS5A inhibitor	-	-