Hepatitis C bubble continues to grow

As deals for pre-clinical stage assets go, they do not come much bigger. The $60m upfront that Vertex Pharmaceuticals has handed to Alios BioPharma today for rights to two pre-clinical hepatitis C candidates, highlights burgeoning expectations in the field and the Massachusetts company’s desire to protect and extend its commercial and pipeline franchise of novel hep C agents.

The deal, which has a staggering bio-dollar potential value of $1.53bn, sees Vertex snap up two polymerase inhibitors, a class of drug very much seen as the future beyond the recently approved protease inhibitors (EASL - Beyond protease inhibitors hep C pipeline filling up, April 4, 2011). Deals of this size and nature, topping the pre-clinical deal league (see below), are normally the domain of promising cancer therapies, indicating intense competition in the race to develop safer and more effective hepatitis C treatments.

Holy grail

Established four years ago, privately-held Alios has completed pre-clinical work on two nucleotide polymerase inhibitors, called ALS-2200 and ALS-2158, which offer the potential to overcome some of the challenges that protease inhibitors face.

Although a major step forward in the treatment of hepatitis C, oral protease inhibitors such asVertex’s own Incivek (telaprevir) and Merck & Co’s Victrelis (boceprevir) still rely on a combination treatment regimen with injectable interferons which can cause nasty side-effects, are prone to viral resistance and treat a limited proportion of hepatitis C patients.

Despite the fact Incivek and Victrelis are not yet fully launched, much attention in the field is turning to the next generation of therapies, and polymerase inhibitors are seen as the next big wave.

Pre-clinical studies indicate that ALS-2200 and ALS-2158, which inhibit replication of the hepatitis C virus by acting on the NS5B polymerase, have a high barrier to drug resistance and the potential to be dosed as a once-daily oral pill.

The fact the compounds are slightly different – ALS-2200 is a pyrimidine nucleotide and ALS-2158 a purine nucleotide – means there is the potential to use them as a dual nucleotide combination in their own right. And with combination hepatitis C therapies seen as the future, attempting to mimic the huge advances made in treating HIV with combination regimens, there is also potential to test Alios’ drugs with Incivek and Vertex’s own polymerase inhibitor, VX-222.

In vitro studies have shown synergistic effects with both ALS-2200 and ALS-2158 in combination with Incivek and VX-222, and also indicate the Alios compounds will work across all genotypes of the hepatitis C virus – Incivek and Victrelis and most late-stage pipeline candidates are effective only against genotype 1, the main strain found in the US, so targeting genotypes 2, 3 and 4 offers greater global treatment of the virus.

Big deal

Following on from the $60m upfront fee, Vertex will also pay $35m on the start of phase I trials for both candidates by the end of this year. If both products gain approval, Vertex will have paid a further $680m in milestones and will also potentially fork out $750m in commercial milestones, as well as royalties on product sales.

As the table below shows, this is the biggest deal for a pre-clinical product since Bristol-Myers Squibb licensed two programs from Exelixis last year. The Alios deal gives Vertex rights to further polymerase inhibitors that may emerge from their partnership, similar to the options that all the other big pre-clinical stage deals also cover.

The high deal price also reflects huge expectations and valuation currently being placed on Pharmasset’s portfolio of phase II candidates, including its polymerase inhibitor, PSI-7977. Pharmasset’s shares regularly
break record highs and value the company in excess of $4bn, seriously impressive for such a mid-stage company.

The high price could also be a result of high interest and competition for Alios’ assets – three of the company’s four main investors are the venture capital arms of big pharma. Alios completed a $32m series A financing round in 2009 from a syndicate of Glaxo’s SR One, Novartis Ventures and the Roche Venture Fund, as well as Novo Ventures.

Should the potential in Alios’ products covert into commercial reality, Vertex could really have executed quite a coup by capturing such prized assets from under the noses of big pharma. Although the corporate VC arms of Glaxo, Novartis and Roche are not supposed to be strategic, should this happen there may well be serious questions asked by their parent companies as to why the opportunity slipped though their nets.

Meanwhile the race to develop a convenient, oral, interferon-free, combination regimen which treats a wide range of hepatitis C patients, which can also overcome inevitable viral resistance issues, continues to gather pace.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Deal Year</th>
<th>Product</th>
<th>Company</th>
<th>Deal Partner</th>
<th>Upfront Fee ($m)</th>
<th>Total Deal Value ($m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2011</td>
<td>ALS-2200 + ALS-2158</td>
<td>Vertex Pharmaceuticals</td>
<td>Alios BioPharma</td>
<td>60</td>
<td>1,525</td>
</tr>
<tr>
<td>2</td>
<td>2010</td>
<td>XL475 + ROR Antagonist Program</td>
<td>Bristol-Myers Squibb</td>
<td>Exelixis</td>
<td>60</td>
<td>565</td>
</tr>
<tr>
<td>3</td>
<td>2010</td>
<td>OMP-18R5</td>
<td>Bayer</td>
<td>OncoMed Pharmaceuticals</td>
<td>40</td>
<td>428</td>
</tr>
<tr>
<td>4</td>
<td>2007</td>
<td>11beta-HSD1 inhibitor</td>
<td>Boehringer Ingelheim</td>
<td>Vitae Pharmaceuticals</td>
<td>37</td>
<td>337</td>
</tr>
<tr>
<td>5</td>
<td>2010</td>
<td>h224G11</td>
<td>Abbott Laboratories</td>
<td>Pierre Fabre</td>
<td>25</td>
<td>not disclosed</td>
</tr>
</tbody>
</table>