Event - Incyte, Lilly forge ahead with second RA JAK

Joanne Fagg

The second of Incyte’s JAK inhibitors, the Eli Lilly-partnered LY3009104, will report early phase IIb data in rheumatoid arthritis (RA) next month, an important moment in determining the value of the Delaware company’s pipeline. The data will give the first signs of how the compound will stack up next to Pfizer’s RA JAK tofacitinib, which will likely have a two-year head start.

With strong expert support for tofa, it appears specialists and regulators are growing comfortable with the novel approach to treating the autoimmune disorder (Pfizer’s JAK inhibitor gets backing for broad RA label, May 10, 2012). There seems little doubt that RA sufferers will be dosed with a JAK well before the end of the year. But a slow ramp for tofa is expected as safety data accumulates and physicians and payers determine where to position it in relation to biologics; thus a second-to-market product with strong data could compete well.

<table>
<thead>
<tr>
<th>Company</th>
<th>Eli Lilly</th>
<th>Incyte</th>
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<tbody>
<tr>
<td>Product</td>
<td>LY3009104</td>
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<tr>
<td>Market cap</td>
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<td>Product NPV</td>
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<td>% of market cap</td>
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<tr>
<td>Event type</td>
<td>Phase IIb results</td>
<td></td>
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<tr>
<td>Date</td>
<td>June 8, 2012 (EULAR)</td>
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Signs

Lilly has completed the six-month dose ranging study of LY3009104, and data from the first three months of the six-month trial will be presented June 8 as a late-breaker at the EULAR rheumatism meeting in Berlin. The 270 patients already taking methotrexate were dosed with between 1 and 8 mg of LY3009104 daily, and 2mg twice daily, or a placebo; the primary yardstick will be the percentage of patients taking 4 and 8mg who report a 20% improvement in the number of swollen or tender joints after three months of treatment, a measurement known as ACR20.

The second three months of the study included a dose escalation, whilst placebo patients will cross over into active treatment, with further efficacy measurements at periodic intervals and conclusion of the trial. Data from that phase of the study is expected to be presented at the American College of Rheumatology meeting in November.

Whilst comparison between trials is not a true measure of head-to-head performance, there will no doubt be those looking at three month data for both to assess the Incyte drug’s potential. In its pivotal trials, tofacitinib scored ACR20 rates of between 42% and 66%, depending on dosage, time on medication and disease progression.

Because of the relatively small size of their programme so far, Incyte and Lilly probably will not need to match tofacitinib’s efficacy in order to move forward. In its first quarter earnings release, Incyte said they are developing a phase III protocol, a sign they are confident the 12-week data supports advancing the oral compound.

The adcom debate held over tofacitinib will likely influence the design of the LY3009104 pivotal programme – whilst the expert panellists were supportive of a broad label, the relatively small safety data base will likely make many specialists cautious about prescribing tofa until more is known. In general, drugs that disable
immune system malfunctions also make the body vulnerable to infection, and tofacitinib had specific issues with blood lipid elevations and lymphoma risk.

Thus the consensus is that tofacitinib probably will not be used until patients stop responding to a biological drug like Abbott Laboratories’ Humira until a more extensive safety data base develops – even though the adcom backed a broad label that put it on an even footing with the biologicals.

**Trail blazed**

As a first-in-class drug, tofa will do a lot of the hard work of allaying concerns about the class, and should it prove itself on efficacy with no specific safety concerns this will benefit LY3009104, should it make it to market.

According to a survey from Reimbursement Intelligence, only 6% of payers believe oral drugs like tofacitinib and LY3009104 will be used after methotrexate and before biologicals if priced at a premium. Forty-four percent believe patients will need to have to stopped responding to all tumour necrosis factor alpha drugs – a class that includes Humira, Remicade and Enbrel – before tofacitinib will be used.

Thus, even though LY3009104 will not have first-mover advantage, it may not be at such a disadvantage, with Pfizer doing much of the leg work for now. The same applies for AstraZeneca and Rigel Pharmaceuticals Syk inhibitor fostamatinib, which is due to yield phase III data in early 2013.

Much still must be learned about the Incyte/Lilly drug of course but positive phase II data next month should build confidence that it can compete in the oral RA space.

**Trial ID** NCT01185353

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