Why a 2020 spotlight will fall on tafasitamab

The anti-CD19 MAb is Morphosys’s lead pipeline asset, and an imminent filing could see it approved next year.

Many European investors will begin 2020 looking beyond advanced projects like Car-T therapies and T-cell-engaging antibody modalities, and instead focus on a simple, naked antibody. Tafasitamab, an anti-CD19 MAb with an engineered Fc fragment, represents Morphosys’s attempt at taking a project all the way to market itself.

The asset has some hefty expectations behind it, with EvaluatePharma sellside consensus seeing 2024 sales of $661m. It is on track to be filed this year in its lead indication, diffuse large B-cell lymphoma in combination with Revlimid, but it is an ongoing study that is key to unlocking its full potential.

That study is B-Mind, which compares the Morphosys project head to head against Rituxan, both cohorts also getting a bendamustine backbone; on November 18 Morphosys closed up 8% as the sellside celebrated the fact that B-Mind had passed an interim futility analysis.

Rolling filing

Meanwhile, a rolling US BLA has been initiated in a less important setting. Morphosys has yet to announce whether this filing has been completed, but aims to do so by the end of 2019.

The basis for this filing is the L-Mind and Re-Mind studies, the former a single-arm trial testing tafasitamab plus Revlimid, and the latter a separate test designed solely to act as L-Mind’s “synthetic control”.

The use of such a synthetic control is an unusual way of getting around the fact that in efficacy terms Morphosys is currently armed only with a single-cohort trial. The regulator’s view is awaited, and the company argues that it has worked hard to ensure that Re-Mind comprises a comparable patient cohort, and is not simply a way to present the L-mind result in a light favourable to tafasitamab.

A possibly more important point concerns the use of Revlimid as a combination drug. Revlimid’s main use is multiple myeloma, and while the drug was approved for mantle cell lymphoma in 2013, and for follicular lymphoma in combination with Rituxan this year, it is by no means a standard of care.

The bottom line, therefore, is that if tafasitamab does secure an initial approval on the basis of L-Mind this use might not amount to much in terms of sales.
And it is why B-Mind is so important. “We are more optimistic than ever that Morphosys will successfully win the approval for tafasitamab, execute on a robust commercial launch, and proceed to extend tafasitamab’s label for additional indications,” gushed Berenberg analysts recently.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Detail</th>
<th>Result</th>
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<tbody>
<tr>
<td>L-mind</td>
<td>Tafasitamab + Revlimid combo, single-arm</td>
<td>81 subjects</td>
<td>ORR 60%, 34/80 CR</td>
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<tr>
<td>Re-Mind</td>
<td>Revlimid monotherapy as &quot;synthetic control&quot;</td>
<td>490 subjects</td>
<td>Deemed positive on the basis of 76 subjects matched vs 80 in L-Mind.</td>
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<tr>
<td>B-Mind</td>
<td>Tafasitamab + benda vs Rituxan + benda</td>
<td>450 subjects, measuring PFS in all-comers and biomarker defined</td>
<td>Passed futility analysis Nov 2019, recommendation to upsize from 330 subjects; topline data Q1 2022</td>
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Source: clinicaltrials.gov & company disclosures.

However, all is not so simple. Most importantly, after performing its futility analysis the data-monitoring board recommended that enrolment into B-Mind be increased, from 330 to 450 subjects. This is rarely a good sign, suggesting that any benefit is marginal, and rendering the trial underpowered under its original design.

Moreover, this is the second change proposed to B-Mind. Earlier this year Morphosys implemented an additional biomarker-based co-primary analysis in this trial: the specific biomarker agreed on with regulators was low baseline NK cell count in peripheral blood.

That also could be interpreted as a sign that tafasitamab was struggling to show an effect in the all-comers population. If so Morphosys is giving itself two shots on goal, and perhaps this resulted in B-mind lacking the power for both analyses, which is why recruitment had to be increased.

Either way investors now have a clear game plan for tafasitamab, and much of Morphosys’s $4bn valuation is riding on it.