Novartis (NOVN SW)

Oxford Biomedica (OXB LN)

- **Quick take** - We are very enthused about a recent development of Novartis' (NOVN SW) CAR-T Kymriah. The latest data from stage I trials is positive. We think the applicability of the T-charge process (explained below) could significantly increase (up to 30x) the addressable opportunity for Kymriah. To put it in context, a ca.5x increase in Kymriah's revenues would imply annual sales of $2.5bn – which would make it the 3rd largest drug for Novartis. This development augurs well for OXB too, given that it is the sole provider of viral vector for Kymriah. OXB is a high conviction buy with compelling risk – reward attributes at this price point.

- **Refractory ALL market well covered by Kymriah** - Kymriah is a CAR-T construct that binds to CD19 on cancer cells. It was developed to treat refractory B-cell acute lymphoblastic leukaemia (ALL), for which it is the dominant therapy. However, the patient population is modest (c.1,000 new patients diagnosed annually in the United States), and we reckon the market is now fairly saturated – which is also reflected in the slower cadence of Kymriah's sales ($474m '20, $587m '21, $536m '22).

- **Penetrating the market for refractory DLBCL** - Novartis has tried to increase Kymriah's potential, by targeting the refractory Diffuse Large B Cell Lymphoma (DLBCL) market, of which there are c.25,000 new cases annually in USA (a significant increase vs. refractory ALL). Competitors Kite/Gilead and Bristol Myers Squib both obtained FDA approval for their CAR-T products in 2021 (Yescarta and Breyanzi respectively). Kymriah on the other hand failed in the Phase 3 trial, BELINDA. The cause of the failure was due to the fact that the process cycle was too long – 50 days on average, from the time from blood extraction to the CAR-T administration. And as the patients were very late stage, this dramatically affected the outcome. It should be noted that there were no serious side effects and earlier stage patients responded well.

- **Novartis changes tack with T-charge** – Novartis has developed a new process (called T-charge) which dramatically reduces cycle times from the time the blood is drawn from the patient, the T cells treated, and then re-administered to the patient. In the new process, the blood is drawn, and the T-Cells separated and infused with viral vector (from OXB) and re-administered to the patient within 3-5 days without the need for a purification stage and with only one day of expansion. Most of the CAR- T cell expansion occurs within the patient's body thereby reducing the time the cells spend ex vivo. There are 2 significant benefits of this new process over the previous one – 1) a dramatic reduction in process times – from 7 weeks, to less than three days; 2) T – charge helps to preserve the naive and stem cell memory T cells, which is expected to result in longer CAR-T cell persistence, and in turn higher response rates and longer durability of the response. The expansion is very fast and much longer lasting, avoiding "tired T-cell" effects.

- **YTB323 and PHE885 – 2 arrows in Novartis' CAR-T quiver** – Novartis has two phase II drugs under development. Both use the T-charge process and have been extremely effective in phase 1 trials. YTB323 targets refractory DLBCL and refractory multiple myeloma (MM), whilst PHE885, a BCMA-directed (B-cell Maturation Antigen) targets relapsed or refractory MM. The early results for YTB323 are very encouraging - and preliminary results have now been released with a Complete Response Rate (CRR at month 3) of 73% for refractory DLBCL and 100% for refractory MM. PHE885 had an impressive 93% Overall Response Rate in Phase 1. Given the multiple indications, the addressable patient population expands significantly – from ca.2000 for refractory ALL (in the US) to c.60,000 in the US– a 30x increase.

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- **Financial implications for OXB** – we are optimistic, given that both YTB323 and PHE885 are entering phase 2 with strong phase 1 results. We expect that NOVN will continue to leverage its know-how and experience with Kymriah and use OXB's platform and processes for the supply of viral vector. We estimate that at present, OXB derives c.£14-15m of PBT from Kymriah – which comprises a low single digit royalty on Kymriah revenues + manufacturing revenues (also low single digit as a % of Kymriah's overall revenues). We posit that even without a royalty stream, the manufacturing revenue could be substantially higher than what it is. The addressable pool of patients is 30x higher – and this is just 1 market – the United States. Assuming that Kymriah captures only 1/3 of market share in the US, and from that target pool 50%-75% of the patients are treated, that is still a potential 5x – 7.5x increase in manufacturing revenues for OXB. That could result in a huge PBT bump of c.£30-45m. There could be further upside to manufacturing revenues, as other countries approve the drug for multiple conditions.

- **Potential for 15%-30% upside (probability adjusted)** - Assuming a target multiple of 10x-15x, we see a valuation uptick of £240m at the low end of the range, to £540m at the upper end. Adjusting the probability of success to 25%, given the drugs are in Phase 2, the probability adjusted market cap accretion is £60m - £135m – c.15% - 30% uptick vis-à-vis OXB's current market cap.

- **OXB as an acquisition target?** - If Kymriah's next version were successful and scaled into a multi-billion dollar drug, we could envisage a scenario in which OXB's strategic importance to Novartis rises manifold. At that juncture, either of 2 scenarios could play out – 1) OXB becomes a valuable acquisition target for Novartis, especially given its current modest valuation. 2) OXB utilises the cash flow and the cachet of producing Kymriah related vector to invest in more process know-how and becomes a dominant C&GT vector producer – which would then reflect in better negotiating power with drug manufacturers and result in higher prices and higher margins. The intrinsic appeal of OXB lies in the fact that as it becomes a CDMO player of choice, given it is a very small (from a financial perspective) but crucial (from a manufacturing perspective) player in the overall value chain, its margins could rise substantially. Either scenario suggests potential for a meaningful appreciation in OXB's share price.

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