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Raising The Stakes: Immunocore's Next Play

by Jo Shorthouse

Two years into her tenancy as CEO, Bahija Jallal is on the cusp of taking UK biotech Immunocore from a research and development organization to a company with a burgeoning pipeline and a marketed therapy. She talks to *In Vivo* about validating the platform, an IPO and creating a commercial footprint.

A lot of people questioned Bahija Jallal's decision to join the UK independent biotech *Immunocore, Ltd.*as its CEO in January 2019. She was installed as the highly regarded leader of *AstraZeneca PLC*'s biologics R&D arm, *MedImmune LLC*, which coincidentally ceased to operate in just a month later under the auspices of its parent company's restructuring.

The Oxford-based biotech was a "diamond in the rough" she told *In Vivo*, "they could not see what I saw in Immunocore," she explained. "The science is outstanding, everything else I thought could be fixed. We have turned it around in two years."

MedImmune had a very bold vision, which prepared Jallal to come to Immunocore, where she once again set a bold vision in the knowledge that people always rise to the challenge. She had learned to make the impossible possible at MedImmune, and has brought this energy to Immunocore. Jallal's vision is "a big part of the job", she explained. To see what is possible.

Platform Validation

Two years later, and Jallal's vision is starting to pay off. The company's science is based on its T Cell Receptor (TCR) technology platform, ImmTAX, which activates T cells to target and kill tumor cells. The company has a pipeline of drugs in oncology and infectious diseases, with tebentafusp the most advanced. Recent Phase III data has gone a long way to validate and de-risk the platform.

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Tebentafusp is a bispecific fusion protein that redirects T cells to kill tumor cells expressing the gp100 protein. Having just completed Phase III trials for metastatic uveal melanoma it has been granted breakthrough therapy designation, and orphan drug designation. In August 2021, the FDA accepted Immunocore's BLA application on a priority review basis, with an expected PDUFA target action date of February 23, 2022.

In July, the European Medicines Agency granted tebentafusp accelerated assessment procedure for the Marketing Authorization Application. Accelerated assessment potentially reduces the time frame for the EMA Committee for Medicinal Products for Human Use (CHMP) and Committee for Advanced Therapies (CAT) to review a MAA for an Advanced Therapy Medicinal Product (ATMP).

Metastatic uveal melanoma typically has a poor prognosis and there is no accepted optimal management or treatment. If approved, tebentafusp would be the first new therapeutic for uveal melanoma in 40 years.

BAHIJA JALLAL

Phase III data revealed in April at the American Association for Cancer Research (AACR) showed just how impactful the drug could become. Compared with available standard therapies, including immune checkpoint inhibitors, tebentafusp nearly halved the risk of death among patients with metastatic uveal melanoma, the first overall survival evidence for any bispecific in solid tumors. However, the data also revealed that the platform can work regardless of tumor mutational burden, and with hot and cold tumors.

This evidence makes it possible to address new areas of unmet medical need, where checkpoint inhibitors do not work in cold tumors, for instance, or the possibility of therapeutic combinations. "It opens up a lot of avenues for us from the biology point of view and from the opportunity point of view," said Jallal, confirming to *In Vivo* that Immunocore is looking at possibilities for tebentafusp beyond uveal melanoma.

Michael Yee, equity analyst at Jefferies, conservatively estimates that tebentafusp could make around $200m per year depending on its price point. "I think it's good to get our feet wet in this one because it's an orphan indication, so we're starting smaller," Jallal said. "The aim is very much to prepare and do the commercialization ourselves in the US."

Virtual IPO

The UK biotechnology industry is on the "cusp of a golden age" according to the UK trade body BIA, driven by strong demand from global investors for UK innovation. There was £1.56bn invested in the industry from March to May 2021, the highest total amount recorded for a quarter since the trade association began recording this data.

As of August 2021, £2.39bn had been raised, compared to £2.81bn in the whole of 2020, which was a record year for investment. Immunocore's IPO raised $297.1m for the company coffers and valued the company at $1.4bn when the trading bell rang on 25 February, 2021. It is in good company as fellow UK biotech companies Adaptimmune and Achilles Therapeutics raised $258m and $176m, respectively.

"I'm a firm believer in play hard and work hard. We did everything we could to celebrate virtually," recalls Jallal. "Once we can get together again, we have a lot to celebrate so we will celebrate even more."

With British firms such as *Kymab Ltd.* and *GW Pharmaceuticals plc* the target of takeover bids, Oxford-based Immunocore is now leading the pack of UK independents. "I think the science in the UK is outstanding, there is no doubt about it. There are a lot of small companies so starting up is not a problem in the UK, it is very entrepreneurial in that way. But then it dries up when you mature these companies, and this is the challenge," said Jallal.

This is the very task Jallal took head on, to grow the company beyond the good ideas. After a series B and C fundraising, the subject of taking the company public was addressed. The best option was to be in the NASDAQ like 99% of its peers, Jallal explained to *In Vivo*. "That really worked for us, in agreement with the board, and I think we had a successful IPO, we are very happy with that. But most importantly we have investors that really are looking at the long term and know this space very well."

Could Immunocore be a bellwether for the UK biotech big hitters? With the Phase III success of tebentafusp, the first product developed using the firm's T-cell receptors technology platform, ImmTAX, approval and commercialization success is there for the taking. Jallal says she takes the role of being a leader in UK science very seriously. "I would love for Immunocore to pave the way and show that it is possible for a UK company to mature that science and bring it all the way to patients," she said. The company will continue to do more UK collaborations, as giving back is something that Jallal is passionate about.

The Next Chapter

"Now that we have validated the platform, there are a lot of possibilities," Jallal told *In Vivo*. The company has key Phase I/II programs in oncology; off-the-shelf therapeutics to counter the PRAME and MAGE-A4 antigens. These programs are expected to provide data by the second half

of 2021 and 2022, respectively.

In the second quarter, the company continued to dose escalate both IMC-C103C (an ImmTAC molecule targeting a MAGE-A4 antigen in patients with solid tumor cancers including non-small-cell lung cancer , gastric, head and neck and ovarian cancers, and synovial sarcoma) and IMC-F106C (an ImmTAC molecule targeting a PRAME antigen, in patients with multiple solid tumor cancers). PRAME is overexpressed in many solid tumors including NSCLC, SCLC, endometrial, ovarian, melanoma and breast cancers.

Early pharmacodynamic data indicate that both IMC-C103C and IMC-F106C monotherapies are demonstrating biological activity at the doses under evaluation.

The company is also looking at the platform being used for infectious disease. In Q2 it initiated dosing in the IMC-I109V global Phase I single ascending dose trial. IMC-I109V is the first candidate in development using Immunocore's immune-mobilizing monoclonal T cell receptors against virus (ImmTAV) platform to enter clinical trials. IMC-I109V targets a conserved hepatitis B virus envelope antigen and is being developed as a potential functional cure.

"It's just the start," said Jallal. "That platform can be very exciting and very modular."

As Immunocore now pushes onto the next chapter, preparing to commercialize its first therapy, Jallal is in her element. She described strategizing as the fun part of her job, the part she likes the most. The team, with the board, is actively working on its long-term strategy she said. Two years ago, when Immunocore was purely a research organization, Jallal took the helm and shored up the clinical and regulatory teams as her priority. There was no commercial footprint then, but now the spotlight is firmly on the launch phase. "For me, it's like a relay. Everybody is just passing the baton to each other," she said.

Paying It Forward

Jallal has had a successful career in the biopharmaceutical industry. Born in Morocco, the first generation of women in her family to go to college, her driving force is a very personal one. She earned a master's degree in biology from the Université de Paris VII in France, and her doctorate in physiology from the University of Pierre & Marie Curie in Paris. She conducted her postdoctoral research at the Max-Planck Institute of Biochemistry in Germany.

She moved to the US and worked at Sugen, followed by Chiron Corporation, serving as vice president of drug assessment and development before establishing the company's translation medicine group. She joined MedImmune as head of translational research in 2006, ultimately leading the company's R&D through an explosion of innovation, taking its pipeline to more than 120 assets. AstraZeneca snapped up the company in 2007 for £15.2bn.

When asked if she believed the same thing may happen at Immunocore, Jallal was coy but honest. “This should never be a goal, because if you want to build something successful, you have to really focus on what is important, which is the science and how we bring this medicine to patients. Then things progress from there, and that’s really what we're focusing on. It’s very important to me.”

However, partnership and collaboration are vital. “They should be part always of your business plan because innovation doesn’t happen in a vacuum. There is not one single institution that has all the innovation of the world. Collaboration and taking advantage of the ecosystem is really important,” she explains.

Women in leadership is a passion of Jallal’s. She served as president for the Association of Women in Science and as an advisory board member and “Woman of the Year” of the Healthcare Business Women’s Association. She was named one of *FierceBiotech*’s “Women in Biotech” and one of the “Women Who Mean Business” by the *Washington Business Journal*. A mother to two daughters, she has a thirst for educating girls early in their school years so that the sciences are a realistic and exciting place to have a career.

When asked if she thinks in 2021, we should still be talking about women in leadership rather than just leaders, she answers confidently that the discussion must continue because the numbers do not lie. There are still not enough women in leadership. “While there is a little bit of movement, it’s not there yet,” she says. “I think it’s a shame because we are not taking advantage of 50% of the population.”

However, the discussion must move onto diversity in general, she says. “Because we are in the business of innovation and having diversity of thought is really important. It is sad, but we still must talk about it and hopefully that’s where I focus my attention next.” (Also see "*MedImmune's Bahija Jallal On Changing The Diversity Narrative*" - Scrip, 15 May, 2017.)

Jallal describes her leadership style as visionary, compassionate and being a risk taker. Looking back at her illustrious career, Jallal highlighted that she will be most proud of her involvement with bringing better medicines to patients. “That’s the most important thing for me, and why I do what I do,” she explains.

“I hope that I would have contributed to bring the next generation of leaders to leave the world a better place,” she said with a smile. “And then of course, in doing so, having a successful business is just the icing on the cake.”