Commentary: Sean Morgan-Jones

J.P. Morgan: Riding the RNA wave – virtually

The decision by organisers of the 40th J.P. Morgan Health Care Conference to go entirely virtual at relatively short notice was understandable but disappointing to many, including myself. As an executive search professional, J.P. Morgan is the biotech equivalent of the World Economic Forum in Davos, Switzerland – a chance to connect great science with the people who make this possible.

Still, virtual partnering can work and this year it was easy to discern the main themes. They were the pandemic, industry partnerships involving new technologies, especially RNA, and a decline in biotech share values on Nasdaq.

The longevity of the pandemic continues to be an issue. Scientists are not yet able to say whether there will be more variants of the SARS-Cov-2 virus and if so, how powerful they will be. Nevertheless, conference participants were clearly hopeful for a fast transition from pandemic to epidemic and a return to normal business activity.

Companies that responded early to the pandemic, but were not successful with vaccines or therapeutics, want to move on quickly to other programmes. Those that were successful, including Moderna Inc and the Pfizer-BioNTech partnership, want to leverage this success with new RNA-related projects. For example, Moderna announced a collaboration with Carisma Therapeutics Inc at the conference to develop *in vivo* engineered chimeric antigen receptor (CAR) monocyte therapeutics for cancer. Carisma will join up its macrophage technology with Moderna's messenger RNA (mRNA) and lipid nanoparticle (LPN) platform to create the new cancer therapies. Carisma will receive $45 million upfront, plus undisclosed milestone payments.

The new focus on RNA, and a preference for partnering over outright acquisition, was illustrated by a deal between BioNTech SE and the UK biologics company, Crescendo Biologics Ltd. Under the agreement, BioNTech will pair its mRNA platform with Crescendo's antibody domain technology to discover therapies for cancer and other diseases.

For its part, Pfizer announced three deals with an RNA component. A research collaboration with Beam Therapeutics Inc will focus on *in vivo* base editing programmes for rare diseases of the liver, muscle and central nervous system. Beam will contribute mRNA and the LPN delivery of base editors to target organs, while Pfizer will help with development and manufacturing. Beam will receive $300 million upfront with potential milestone payments amounting to $1.05 billion.

Pfizer also announced a deal with Acuitas Therapeutics Co of Canada giving it an option to in-license Acuitas' LPN technology for up to 10 targets for use in mRNA vaccines and therapeutics. This is the same delivery technology used in the Pfizer-BioNTech Covid-19 vaccine. Finally, to further strengthen its mRNA platform, Pfizer concluded a deal with Codex DNA Inc giving it access to technology for constructing synthetic DNA, RNA and proteins, potentially speeding up development of mRNA-based vaccines and therapeutics.

In the build-up to the annual J.P. Morgan meetings, investors often speculate about which companies will announce mega-mergers. They weren't disappointed in 2019 when Bristol-Myers Squibb Co announced plans to acquire Celgene Corp for a massive $74 billion. A few days later, Eli Lilly and Co disclosed an agreement to acquire Loxo Oncology Inc for $8 billion. This year, there were no mega-mergers in terms of dollar values. This was surprising given the war chests built up by Pfizer and Moderna from their Covid-19 vaccines. More likely, these companies will disclose their spending plans at a later date.

Amongst the deals of note were a collaboration between BMS and Century Therapeutics Inc to develop up to four induced pluripotent stem cell (iPSC) derived engineered natural killer cell and/or T cell therapies for haematologic malignancies and solid tumours. The upfront payment is $150 million, with an additional $3 billion in milestone payments. Separately, Bayer AG and Mammoth Biosciences Inc signed a gene editing deal focused on liver-targeted diseases valued at potentially more than $1 billion. Finally, Amgen Inc and Arrakis Therapeutics signed a deal which they said is potentially valued at "several billion dollars" to develop RNA degrader therapies. These are small molecule drugs that destroy RNAs encoding disease-causing proteins by inducing their proximity to nucleases.

Do all roads necessarily lead to Nasdaq?

The final quarter of 2021 was difficult for biotech companies listed on Nasdaq. Market capitalisation figures published in *MedNous* for 56 European companies listed on the US exchange showed that 41 declined. This trend was mirrored across the wider market. Equity analysts have offered several explanations. The new US administration appears set on a stricter enforcement of competition policy which could affect merger and acquisition activity. Inflation affects pre-revenue biotech companies by introducing a greater level of risk into the valuation of future milestone payments. Finally, the market for initial public share offerings has, by many accounts, become too speculative. Many biotech companies going public are pre-revenue and have not even reached the proof-of-concept stage for their technologies.

One senior J.P. Morgan analyst pointed out that market valuations based on the traditional clinical trial paradigm, which means judging a company on the basis of the data it generates, were being trumped by preclinical platform technologies and charismatic chief executives. The market retreat therefore could be seen as a healthy correction.

Let's hope that in January 2023 we will all be back in San Francisco in person to find out.

This article was prepared by Sean Morgan-Jones, Chief Commercial Officer at Morgan Prestwich Executive Search.

