Biotechs: Proving that prevention really is better than the cure

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Background

The global healthcare sector has undergone significant change over the past 20 years, largely driven by advances in the dynamic biotech sector. Involved in such things as antibody therapies, protein engineering, gene editing, immunology and diagnostic tools, to name a few, the biotech industry has made an indelible impact on our lives.

My fascination with science and biotech started in my biology class in high school in my hometown of Dreieich, near Frankfurt, Germany. The onset of AIDS and HIV attracted me to the world of molecular and cell biology. The HIV virus has a pretty simple life cycle, but it knows how to hide and create havoc. I went on to study virology and molecular biology at the University of Tübingen, Germany and at the University College London, and was fortunate to work on a HIV drug at Novartis that gained approval in 2003.

My time in the pharmaceutical and biotech industry taught me that facts drive decisions and, together with a dedicated team of scientists ("drug champions"), can overcome preconceived opinions and challenges. In this industry, you cannot be complacent or rely on a spreadsheet. Everyone, from the CEO to the bench scientist, is required to keep an open mind — let facts tell the story rather than emotions (very similar to investing, actually). What may be the key franchise for a company today, may not be the right place to be in five years' time.

Take HIV as an example, today, less than a handful of companies work on anti-HIV drugs, the focus has shifted to other diseases and different therapeutic approaches. As one chapter closes another one opens. The large French pharmaceutical company, Sanofi, for instance, recently announced it is exiting cardiovascular and diabetes research — therapeutic areas that were once the company's bread and butter.

A constant process of reinvention

The drug development industry has to challenge itself and evolve every day, which makes it a treasure trove for investments. Drug patents only last for a finite period, and when they expire the next generation of products need to come through. Companies know when their loss of exclusivity on a particular product will occur, and hence they need to plan accordingly. Again, in very simple terms, it is not that dissimilar to funds management. Investments are like "pipeline drugs" that need to be reassessed on a regular basis. At times, the investment case changes and the opportunity no longer exists. In other instances, the hypothesis is playing out and more money needs to be invested.

Besides monitoring the portfolio, innovation continues, and hence new investments need to be assessed frequently. This is particularly true for large drug developers — and here the biotech ecosystem offers a myriad of opportunities.

Biotechs are all about pushing the envelope of innovation and raising money to test a scientific hypothesis. There will be hype and there will be neglect, but keeping the bigger picture in mind will facilitate navigation through the maze of emotions.

Innovation is at the core of the industry and it never ceases to amaze me how determined scientists are in the face of failure. While it may seem counterintuitive, failure is a key part of this industry and it offers tremendous investment opportunities when the science and people are right.

Twenty years ago, genomics was all the rage with the human genome being sequenced. The ability to identify the order of the four "building blocks" that make up our DNA was a major breakthrough in medical science.

While, the initial promise of making drug development more efficient fizzled out (causing the biotech bubble to burst at the time), importantly, it was the start of an evolution of sequencing technologies. Understanding the sequence of a person's DNA enables faults (eg, mutations) to be identified in their genetic make-up, allowing earlier detection of disease, which is the holy grail in medicine.

Today, it is all about applied sequencing and making it affordable to a wider audience. The total cost of the Human Genome Project, which took 13 years in total, was US$2.7 billion. It now costs individuals in the United States a lot less; in the cancer diagnostic setting, sequencing and the subsequent analysis will cost about US$10,000-$15,000. A report with the results will be available within weeks. Often lower prices for genome sequencing are quoted but they fail to account for the very rigorous analysis that is required in a medical diagnostic setting.

No doubt, however, costs of genome sequencing continue to decline and more biotechs are being founded, offering diagnostic services that profile cancers, identify rare diseases or determine inflammatory disease profiles. In years to come, healthcare will shift towards the prevention of diseases rather than waiting for symptoms to appear. A key element for this shift to occur is technology innovation.

The molecular biologist toolbox continuously evolves, with gene editing (where DNA is inserted, deleted, modified or replaced, with the goal of curing certain genetic diseases) currently one of a number of tools in the limelight. It is these tools in the laboratory that foster innovation in drug development. Technologies are available today that allow scientists to drill deeper into the network of a cell at an almost industrial scale. Combine that with sophisticated data analytic tools, and scientists can delve deeper into the complexity of a disease.

As a consequence of this scientific work, segmentation of diseases is occurring, and new drugs are being developed for different sub-segments. Oncology is the classic example, whereby a tumour is no longer labelled by its location, it is now about the molecular make-up of the tumour that will determine the treatment approach. This is the hallmark of precision medicine.

The evolution of diagnosis and treatment of lung cancer is a case in point. Lung cancer used to be treated with surgery, chemotherapy and radiation. While this is still the case today, there is a rapid move towards precision medicine. Today, molecular tools are applied to detect mutations (of which there

are many) in a lung tumour biopsy. (One day, we may even be able to diagnose lung cancer via a blood sample, which biotechs are currently working on.) In addition, a pathologist will also determine the level of inflammation of the tumour cells as well as the surrounding environment. The resulting molecular profile, rather than the location of the tumour, will then guide the oncologist to what drug or drug cocktail is best to use. The number of different types of mutations identified for lung cancer continues to expand (as depicted in the diagram) and so is the therapeutic armamentarium of an oncologist, as each mutation requires a different drug with each developed by a different biotech.

The number of identified lung cancer mutations continues to expand

Our understanding of the role of the immune system in oncology has added another dimension to how a tumour should be treated. The activity in the field of immuno-oncology is immense, ranging from small molecules to cell therapy. The latter, for example, manipulates the "soldiers" of the patient's immune system, so-called T cells or Natural Killer cells, to seek out a specific cancer and destroy it. Again, it is thanks to molecular biology and biotechs that these significant advances have been made possible, resulting in improved life expectancy.

Biotechs as well as academia sit at the forefront of these innovations, with one biotech working on one mutation, another developing new cell therapies, while yet another focuses on developing a diagnostic test for molecular profiling.

Increasing collaboration driving innovation

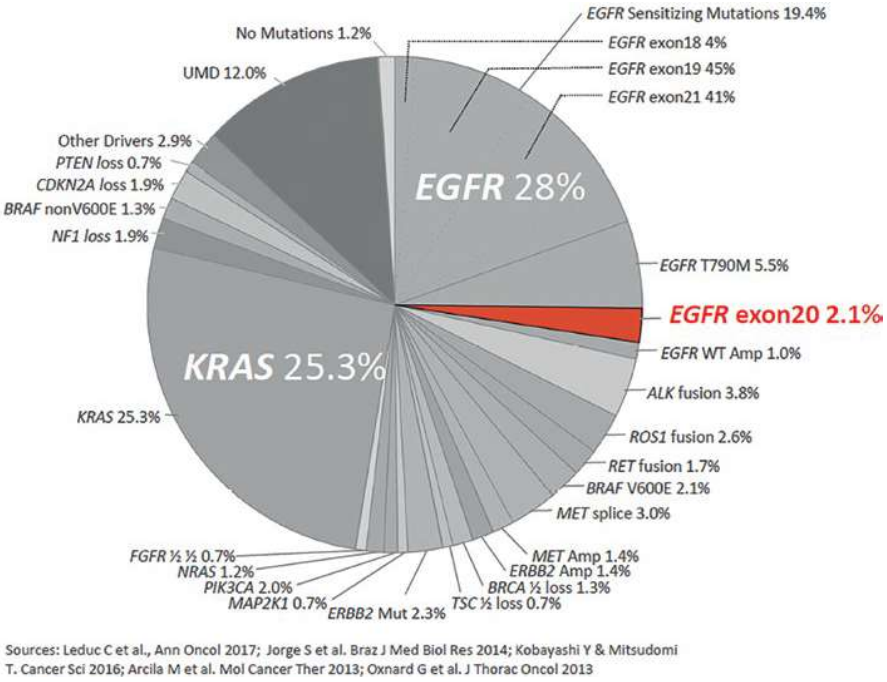
The breadth and depth of the healthcare sector has expanded significantly. A recent article in the journal, *Nature Reviews Drug Discovery*, highlighted that sponsorship of clinical trials is changing, with biotechs playing a greater role. In 2000, 50% of phase 1-3 trials were sponsored by the top 10 pharma companies. In 2017, it had fallen to 27%. That's quite astounding.

Biotechs are the R&D engine of tomorrow, even a large, well-established company like Roche, which has a powerful internal biotech culture, looks externally for help. Johnson & Johnson, similarly, wholeheartedly encourages external innovation by running innovation hubs called JLABS.

It is impossible for pharma companies to fund all the new innovation that is occurring, while at the same time launch new drugs globally. Biotechs have a crucial role to play in this ecosystem. Not only is their entrepreneurial thinking more suited for new innovation versus the bureaucracy of a large organisation, biotechs are able to access capital from venture capitalists, often involving the venture capital arms of pharma companies as well. For pharma companies, it is important they manage their R&D budgets correctly and not fall into the habit of funding the same internal research that they will later acquire. For investors, it is as critical to understand how the business development team functions, as it is to understand the internal pipeline of a company.

The growth in biotechs has created investment opportunities not just for venture capitalists, but also for fund managers, with Platinum an active investor in the global biotech sector. We do not shy away from these early-stage investment opportunities. While we do invest predominantly in global companies, there have been a number of attractive investment opportunities in Australian biotechs that we have invested in.

As mentioned earlier, there is a high risk of failure in this industry, however, having a background in this field certainly helps when delving deeper into the science — knowing ***what*** questions to ask and, importantly, ***who*** to ask are critical. Healthcare is a people business. If the core of the company, technology and team is right, "failures" can often be the best investments, as the companies have to "dig deep" to prove themselves and restore investor confidence.



Sources: Leduc C et al., Ann Oncol 2017; Jorge S et al. Braz J Med Biol Res 2014; Kobayashi Y & Mitsudomi T. Cancer Sci 2016; Arcila M et al. Mol Cancer Ther 2013; Oxnard G et al. J Thorac Oncol 2013

Diagram sourced from Takeda R&D presentation, November 2019

While the technology sector is familiar to many investors, we believe biotech will be the sector to watch this decade and beyond. Innovation is thriving globally, and China is embracing novel drugs at a rapid pace, adding a geography that is only just starting on its modern medicine journey.

Over the next decade we expect the healthcare sector will experience significant changes in terms of novel therapeutic approaches, but also changes to how healthcare is delivered. The convergence between tech and biotech will make for a very interesting period ahead for investors in this exciting and dynamic sector. E

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