Just What The Doctor Ordered

Early on in Lindsell Train's history Nick and Michael looked seriously at investing in leading pharmaceutical companies, but came to the conclusion that at that time they were materially overvalued. In the UK Glaxo, for example, was on an enterprise value to sales multiple of over 8x. We have continued to keep the pharmaceutical industry sector under consideration given there are a number of aspects we like. In particular it tends to be an exceptionally high margin industry with potential for very high cash generation. On the downside, however, the patent expiry system (each drug is granted a patent which eventually expires, at which point generic manufacturers are poised to launch their own, much cheaper version) means that it is "hit driven", so there is a constant need for reinvention and discovery – more so than for other industries we are drawn to. As yet we have only invested in Japan, where pharmaceuticals continue to trade on lower multiples than their European or US peers. Currently we hold three Japan-based pharmaceutical companies in the Japan fund, of which one, Astellas (bought for 1.3x sales in 2011[1]), is also in our Global portfolios.

More recently, we have become alert to big changes happening within the global pharmaceutical industry. The two key developments are as follows:

1) There is a shift from traditional small molecule "white pill" drugs to biologics. The main effect of this is a change in the economics of these drugs' lifecycles – "white pills" are easy to copy cheaply and at scale, so patent expiries result in an instant 90% drop in sales, but the next generation of biological drugs have a different lifecycle. This is broadly because generic "biosimilars" still need $2.5-5m in R&D spend and generic manufacturers are obliged to test them in the same way as a patented drug, so prices can't be slashed as dramatically as before.

2) Companies are now focusing on a much smaller range of diseases. In the past the pharmaceutical industry functioned like a movie studio where the blockbusters paid for the flops (it has also been likened to the randomness of drilling for oil, where a lot of money is spent on R&D but nobody can be sure of the price of the final product at the end). However, the "low hanging fruit" of diseases with large patient populations have largely all been addressed, and the industry focus is now on developing smaller, specialised products with much smaller patient populations and therefore much higher price tags. One example is Merck's immuno-oncology offering Keytruda, which costs $150,000 per patient per year. Compare this to Pfizer's statin (cholesterol reducer) Lipitor, launched in 1996 and by some margin still the best-selling drug in the history of pharmaceuticals, despite the presence of other statins such as AstraZeneca's Crestor[2], itself a blockbuster. In the USA the population of patients on statins is an enormous 15 million[3], meaning that volumes more than offset its comparatively low price of $2,000 per patient per year.

Against this background of fundamental industry change, it seemed an opportune time to conduct a broad survey of the space and try to identify any possible opportunities. The bulk of the research we undertook involved conversations with each pharmaceutical company in our universe, as well as some that weren't on the list (13 in all). Perhaps the most fundamental question put to each company was, *what exactly is the core asset which allows the company to keep coming up with patentable intellectual property*? This question didn't yield many concrete answers or even consistency. For what it's worth, serendipity or chance combined with a strong balance sheet was often mentioned. But my first observation is that all the companies which have done well recently (both in terms of business and share price performance) credited their early identification of the need for specialisation and targeted R&D into just a few therapeutic areas. Given the shift from small molecule to biologics, with the resulting change in the way patent cliffs work, companies which haven't narrowed their R&D target range down to a core list of competencies and set themselves up as a leader in specific spaces (especially those addressable with biologic drugs) definitely seem to be at a disadvantage. I suspect it's no accident that the highest valued company of all those I've looked at (Novo Nordisk, currently on 6.4x sales[4]) is almost a pure diabetes specialist with 80% revenues from this therapeutic area, and that the second highest valued company (Bristol-Myers Squibb, on 5x sales[5]) targets an extremely narrow range of diseases with a distinct emphasis on biologic oncology. Sanofi, by contrast, actively promotes itself as diversified and is on a much lower 3x sales[6].

My second observation is more of a caution. While attaining (and keeping) a strong position in one therapeutic area is important for pharmaceutical companies, that position doesn't then function like a successful consumer goods franchise which benefits from a durable brand and consumer loyalty. In fact "expertise" rather than

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"franchise" might be a better description: while it's possible for drugs to have a great deal of physician and patient loyalty, ultimately efficacy and value is king and a trusted name alone is no defence against a more effective or cheaper offering. It's vanishingly rare that brand value as a concept is applicable to individual drugs, although on the rare occasions when a drug is successful enough to spawn line extensions and more indications, these can be tremendously valuable. A good example is Johnson & Johnson's Remicade, which has 16 different indications and maintains a 70% market share in Europe despite biosimilars coming to market in 2016. Some drugs (such as the aforementioned Lipitor) do gain consumer recognition, e.g. when there has been a lot of television advertising (permitted only in the US), but the boost or protection this affords is likely to be temporary.

Nevertheless, a stronghold in a key area (e.g. Roche's global dominance in oncology or Novo Nordisk's in diabetes) is the result of years of investment which has resulted in expertise and hopefully a stable of drug "intellectual property". This acts as a moat, as would-be new entrants have to catch up with spending, but more importantly it makes the company a magnet for talent and early stage biotech drugs. New biotech assets are generally not listed and so not accessible via the open market – those firms with promising offerings tend to approach or be approached by big pharmaceutical companies. It's also worth noting that most large pharmaceutical companies no longer predominantly discover new drugs with a team in a lab – a lot of the R component of the R&D budget actually goes on early stage acquisitions and licensing, even if it's booked as research. J&J are very open about this and even cite their early stage collaborations and good 'eye' for a promising new product as a major company strength.

Price regulation is a fact of life for the pharmaceutical industry and we see no indication that this will change. Pricing will probably always be constrained in some way, whether it's direct government action to limit expensive drugs (for example the governing body in the UK will only pay for drugs costing less than £30,000 per patient per year and the Japanese government limits pricing both absolutely and also via their generic target) or indirectly, such as US insurance payers refusing to reimburse for expensive drugs not on their formulary, or list of approved medications. Historically the US has been the most profitable region for drugs companies, but increasing consolidation amongst insurance payers in the US means they are growing more powerful every year. It would be foolish to disregard the impact this will have on drug pricing, especially as pharmaceutical companies target ever smaller patient populations with ever more expensive drugs. Despite these pressures, we nevertheless do think that in the long run efficacy will win out and drugs offering genuine advances in treatment will always be rewarded.

While the rewards of finding efficacious new drugs are enormous, generating prodigious cash flows over a set period of many years, we acknowledge that the risks are commensurate with the potential payoff. In recent weeks this has played out before our eyes: AstraZeneca has reported poor results from Mystic, its landmark lung cancer drug trial, and the resulting hit to the share price was the worst since the company's formation in 1993. AstraZeneca's shares fell 16%, which reduced its market cap by more than £10bn. The 90% fall in Valeant's share price since 2015 is another cautionary tale which fundamentally highlights the risks of its strategy of growth via acquiring "mispriced" drugs and hiking prices. Ideally, pharmaceutical companies would love to grow via a steady stream of in-house new drugs but arguably that strategy may now be harder to follow. The "growth via acquisition" model is a continuum. A model of judicious acquisition can be productive – in recent years Pfizer has grown mainly by acquisition and indeed its attempted takeover of AstraZeneca in 2016 highlighted its lack of in-house opportunities – but at its extremes, e.g. Valeant, the risks of political pushback and payer price intolerance make the model demonstrably unworkable.

Perhaps even more interesting for us than pure pharmaceutical is the over the counter (OTC) healthcare industry, which enjoys more consumer good-like qualities such as a lack of patent expiries and a strong element of brand loyalty amongst consumers. Globally, this is an exceptionally fragmented market that is ripe for consolidation, with only 25% of total sales coming from the top 10 companies. Global market share figures vary according to estimates from all the companies, but Sanofi estimates the 'big pharmaceutical' market shares as Bayer at #1 with 4.5%, GSK/Novartis JV at #2 with 4.4%, Sanofi and J&J tied at #4 with 4.2-4.3% and Pfizer #5 with 3.5%[7]. Reckitt Benckiser probably has 4-5%, putting it at around #4 but given the tiny differences in market share, it is hard to tell. This fragmentation is largely due to the localised nature of the business – consumers trust brands they know well, and since these are often local brand names (whether from a local or global competitor) it can be difficult to truly globalise a product. In addition, countries differ in their approach to self-care – Chinese traditional medicine is very different to Western, for example – and there is the widespread issue of OTC healthcare departments often being part of a larger pharmaceutical company, which means there is a risk they are run for cash but chronically under-nurtured, for example producing little in the way of innovation.

Despite the fragmentation and difficulties with globalising products, the OTC market is an attractive space. Consumer trust and loyalty are crucial, with doctor and dentist recommendations being a key differentiator for

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many products, and strict governmental regulation in all regions means higher barriers to entry and therefore better margins for existing competitors. Structural growth will come from cash-strapped governments increasingly encouraging people to self-medicate, as well as ageing populations and more obesity, which all tend to be treated with more drugs; in some locations, such as the UK, deregulation means that some OTC preparations are available in supermarkets and convenience stores as well as chemists, all of which encourages consumers to opt for OTC preparations as a first line treatment.

We sense that the pharmaceutical industry is at a crossroads. The shift from small molecule drugs to biologics is genuinely revolutionary and, as I touched on earlier, the different pricing mechanics of biologics and biosimilars to small molecule and traditional generics may result in some respite from the patent cliff model. As an illustration, consider what happened when Sanofi's blockbuster Lantus insulin went off patent – just one biosimilar was launched by Eli Lilly, and at a price discount of only 15%. Companies which have grasped the importance of the shift could have 10 (or more) years to do really well, with little competition for expensive, effective products and their initial investments paying off handsomely as others struggle to catch up.

So what have we done as a result of this work? Two names have been removed and one has been added to the global universe, and we are satisfied that all the companies included in the universe are genuinely of interest, both as potential investments and to monitor what happens in terms of OTC consolidation over the coming years. We continue to value our investments in Astellas, Takeda and Taisho (the latter only for its exposure to Japanese and Asian OTC), continue to watch developments within the OTC market closely, and in the long term feel that the pharmaceutical space is probably growing more attractive given the increasing specialisation. We have not yet made any new investments, but we are pleased to have a better understanding of the space and feel that, should a dislocation in value happen within this category (as had happened in Japan when we initiated our three holdings), we are poised to take action.

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Footnotes:
1,4,5,6 Bloomberg
2 "Blockbuster" drugs as defined as having sales of >£1.5bn
3 Instructional Management Systems
7 Figures supplied by Sanofi in 2017

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