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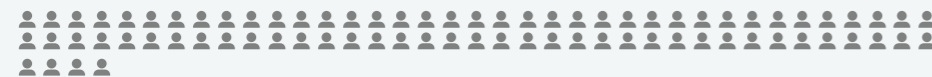
Transforming the pharma business model to prevent lost treatment opportunities and optimize return on investment

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Lost Treatment Opportunity

Oncology patients that could be missed from targeted therapy due to suboptimal testing*

 **6,514 monthly**  = 1000 patients

 **78,168 Annually**

*US only, 13 key oncology biomarkers

Data based on real-time real world assessment from leading US labs and claims data bases, April 2017. Data is conservative based on known testing issues with novel molecular tests and does not include patients NOT TESTED due to lags in test adoption which would likely triple these numbers, making the real potential patient gain to be between 30-50%.

Introduction – Diagnostics are the poor relation in precision medicine

The importance and role of diagnostic testing in transforming healthcare is underestimated. Precision medicine is the term for a therapy (drug) that is tailored via diagnostics to suit the individual patient. A diagnostic identifies which therapy a patient or a subset of patients is most suited to and, crucially, which therapies will not work for them. Ideally, when diagnostics are used appropriately at specific stages of the patient pathway, patients can receive the right treatment at the right time. However, in the real world clinical setting, achieving this synchronization of test and therapy is proving extremely difficult.

Diagnostic planning in support of therapy goals is underway

Where a diagnostic is relevant to the launch of a particular therapy, therapy asset teams are being provided with budgets and resources to assess the level of interdependency between these two technologies and are partnering accordingly. Despite the complex need to incorporate some 400 diagnostic-specific workstreams into the therapy lifecycle planning, many in the pharmaceutical industry have already moved to the 'next generation' of diagnostic planning in support of therapy goals. In fact, in 2015, 36 of the Top 50 selling pharmaceuticals were on the FDA Pharmacogenomics list or diagnostic-enabled, and brought in over \$140bn in revenue.

Our most recent analysis of leading pharmaceutical companies confirms that the integration of diagnostics into the therapy business model is well underway¹. Seventy per cent of the leading brands on the market are dependent in some significant way on the testing ecosystem around it, and **75 per cent of future therapy launches** (from 2020 onwards) **have a specific diagnostic as a predominant feature of the pharma commercial model**. In financial terms, \$200bn in therapy revenue is already dependent upon the diagnostic ecosystem and we estimate that some \$3m per day is being spent on the co-commercialization of diagnostics across the industry.

While some laggard competitors remain on a steep learning curve, most of the top 10 pharma companies have a recognizable centre of diagnostic planning and have awoken to the fact that their technology-centric diagnostic partners—whilst supporting their test development and regulatory goals—are ill-equipped to support the all-important clinical diffusion and laboratory adoption goals. As a result, these therapy teams are having to learn how the diagnostic market can support their assets and fill the gaps in development infrastructure created by an underfunded diagnostic industry.

How much is invested in the diagnostic ecosystem in support of targeted therapy launches?

A targeted therapy launch investment in the US can range from US\$150m to \$200m. The therapy commercial model sees this spend typically go towards publications, guidelines and direct education for physicians and payers, plus direct-to-consumer advertising, social media and advocacy for patients. Today, inclusion of the diagnostic as part of this model sees a 'small' investment of US\$3m to \$12m (approximately 6 per cent of therapy commercial spend) per biomarker applied across these channels but also targeting the laboratory-physician interface (as the physician has a vital communication channel with the laboratory) and direct education between the lab and the diagnostic supplier.

The real potential of diagnostics to transform the pharma model is unmet

As therapy teams seek to achieve excellence in their planning and pre-launch preparation for testing and specifically right-size their investments, it will be important to better understand not just the basics of diagnostic commercialization, but the power of testing to transform the commercial therapy business model and the return on investment in patient share which can be achieved with fully aligned testing and treatment commercialization². The horizon therefore shifts from "How do I integrate testing into the therapy launch?" to "What return should I expect from increased investment to drive better testing alongside our therapy?"

To support this important analysis Diaceutics has leveraged real-time (versus clinical trial setting) US testing data from our laboratory network, focused on 13 known oncology biomarkers, where the greatest number of experience in parallel test and therapy launches exist³. Our analytical framework quantifies the number of patients likely missing out on the right therapy due to avoidable issues with their testing journey. To ensure a fully evidence-based assessment we focused only on the very basics of an efficient testing market, namely turnaround time, test sensitivity and sample management where adequate published references of real-time testing gaps for each biomarker existed. We **did not** include any quantification of the number of patients who should or could be tested (if there were faster test adoption at the physician and laboratory levels) although we speculate in the conclusion the likely impact this might have on our analysis.

What the real world data suggests

The analysis suggests that there is a significant lost targeted treatment opportunity amounting to ~6,500 oncology patients per month or ~78,000 patients per annum in the US alone. These are patients whose test results could have triggered targeted treatment but likely did not because the test results were incorrect, too late or inconclusive due to sample management issues. The **potential lost revenue** to the pharmaceutical industry coming from this cohort analysis would be **\$8.3bn per annum in the US alone**.

We mentioned above that this analysis did not include patients lost to inadequate test adoption in the first three to four years of test launch. When we factor this in, based on real world test adoption curves, the potential lost revenue in the US alone would likely double to \$16.6bn. A similar picture will be found across the five leading markets in Europe, again suggesting that **inadequate investment in quality testing** in support of targeted therapy launches **could be costing the industry a staggering \$32bn in lost therapy revenue per annum**, with a significant impact on patient outcomes.

This real world analysis of lost treatment opportunity remains an ongoing study as we learn more about the differences in how patients are actually tested and treated versus what was observed in a controlled clinical trial setting⁴.

Are current diagnostic commercial investment levels adequate?

In a business model where the importance of optimal testing is clearly recognized and patient-centric policies are the ideal, the question is no longer “Which patients tested positive for a targeted therapy choice?” but rather “**How many of the right patients were not tested and missed the treatment opportunity?**”

Given the size of the lost treatment opportunity arising from underinvestment in the diagnostic ecosystem it is important to better understand the expected level of patient gain which emanates from smarter and greater commercial investment^{5,6,7}. Previously, we have undertaken this analysis retrospectively and it has suggested that for every dollar invested in better diagnostics the pharmaceutical industry can expect between \$30 to \$60 back in additional therapy revenue^{8,9}. Using our real-time analysis, and assuming we can achieve at least a 25 per cent patient gain (based on analogues), we are seeing very similar anticipated return on investment suggesting that the investment in better testing pre- and post-launch can deliver superior and, importantly, relatively rapid returns.

Conclusion

Precision medicine is driving two disparate technologies to converge. The issues and opportunities resident in technology convergence is the subject of much discussion in economic literature, where the common theme is the need to understand the new opportunities which arise by reinterpreting the solution not as ‘two separate’ parallel technologies but as a single solution synergized by integration. It is to this theme we address our important and novel analysis.

Enabled for the first time by access to robust real-time testing data in the US, we can determine the likely patient and financial impact of right-sizing and right-timing the integration of testing into the therapy business model. Our evidence-based assessment suggests that at least 30 per cent of oncology patients in the US are missing out on the optimal therapy due to avoidable quality gaps in testing. In reality, however, this range is likely to be significantly higher (30 to 50 per cent) when we consider the fact that test diffusion (laboratory availability and physician demand) often lags behind therapy demand, and suffers acutely in the early years of novel test introduction from suboptimal physician education, incomplete reimbursement levels, and delayed inclusion in guidelines.

Important questions remain about how to fully leverage the convergence of testing and treatment in the patient pathway. Leaders in precision care accept that earlier testing and treatment has the potential to revolutionize many diseases, and initiatives such as the PM Connective have been established to develop a collaborative approach to healthcare across all sectors through earlier integration of test, treatment and education¹⁰. Analysis of the impact such initiatives will have on disease is still at an early (albeit promising) stage and will be the subject of future economic assessments.

A much more tangible and realizable goal in the short term is to right-size and right-time diagnostic investment so that patients can achieve improved access to the therapies available today. We do not underestimate (and continually observe) the challenge to the pharmaceutical commercial business model of thinking beyond the pill, but we believe this type of economic analysis can provide a route map towards:

1. Accepting the industrial limitations of the diagnostic industry to commercialize the disruptive technologies they are sponsored to develop and the need to look beyond the cash-strapped diagnostic companies for new commercialization approaches;
2. Radically increasing the commercial investment in parallel diagnostic diffusion in a way which accelerates test availability and adoption in step with therapy demand, doing so in the confidence that it will provide high return on investment;
3. Communicating the major patient impact which can be achieved by shouldering greater joint responsibility for converging testing, treatment and education across all stakeholders (such as payers, patient advocacy groups, regulators and professional associations).

Thankfully, we have all moved beyond the era when testing was regarded as a niche adjunct to the therapy business model. Novel biomarker launches are now part of the narrative of most oncology and many non-oncology therapies. However, this next frontier should see us moving past the under-resourced commercial efforts of the diagnostic industry and on to developing new commercial partnering models where test diffusion is provided similar professionalism and timely investment. Pharma CEOs and institutional investors can take comfort from the fact that time spent on this next frontier of precision medicine will deliver even higher return on investment and that our patients will ultimately be the beneficiaries.

Diaceutics is a global group of laboratory, diagnostic and pharmaceutical experts. Our goal is to help pharmaceutical companies integrate diagnostic testing into their treatment pathways. We are empowered through a real-time flow of testing data from our worldwide laboratory network which we use to help our pharma clients understand and leverage the diagnostic landscape.

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10. www.pmconnective.org. The PM Connective’s mission is to drive collaboration and integration across all healthcare industry stakeholders at the disease-specific level in personalized medicine in order to create a new model and valuation framework that will offer clinical and financial benefits in personalized healthcare.