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Valuations in a precision medicine world

Navigating the complexities in precision medicine deals

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Introduction

An increasing number of assets, particularly in oncology, are precision medicines (PMs). Indeed, in 2023 around one-third of FDA-approved new molecular entities were precision medicines. For the purposes of this paper, we will define precision medicine (PM) therapies as those that, after disease diagnosis, require an additional test to determine therapy eligibility. Driven by high unmet medical needs and an unprecedented level of innovation, the precision medicine deal market, whether asset licensing, R&D collaborations, or outright acquisition, continues to attract fierce competition as major biopharmaceutical companies look to address upcoming patent cliffs, fill existing portfolio gaps, or enter new markets. Indeed, 9 of the top 10 deals by dollar value in 2023 in the U.S. had some precision medicine component (see Table 1).

Despite this interest, recent data published by Diaceutics and the Personalized Medicine Coalition suggests that only around one-third of advanced non-small cell lung cancer (aNSCLC) patients who qualify for a precision medicine therapy are actually being prescribed one due to a multitude of issues.[1] So even with precision medicine's "poster child" — lung cancer — we are still not optimizing care delivery. This has significant implications for any pharma company looking to do deals in the precision medicine ecosystem. If the idea that "no test=no patient=no revenue" is true, then companies risk significantly over-estimating their addressable market, with obvious implications for valuations.

As precision medicine continues to advance, including into other areas such as neuroscience, immunology, and across rare diseases, biopharma must address a new set of precision medicine-centric diligence questions that will underpin the deal thesis. In this paper, we will discuss these dynamics, with implications from a valuation perspective.

[1] JCO Precision Oncology, "Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non-Small-Cell Lung Cancer," October 31, 2022

Table 1. Nine of the top 10 2023 biopharma deals by value had targets with a presence in precision medicine, with more than 50 percent of the PM deals being outside of oncology*

Acquirer	Target	Deal month	Deal value	Primary therapy area	Precision medicine component
Pfizer	**Seagen**	March	$43B	Oncology	Seagen has a portfolio of antibody-drug conjugates (ADCs) for various oncology indications.
BMS	**Karuna**	December	$14B	CNS	None
Merck	**Prometheus**	April	$10.8B	Immunology	Prometheus is developing PRA-023 for various autoimmune indications. The asset targets TL1A, and the company is stratifying patients using a companion diagnostic (CDx).
AbbVie	**Immunogen**	November	$10.1B	Oncology	Similar to Seagen, Immunogen brings AbbVie a portfolio of ADCs.
AbbVie	**Cerevel**	December	$8.7B	CNS	Cerevel is developing a portfolio of CNS assets using patient stratification based on disease phenotype (e.g., late versus early Parkinson's).
Biogen	**Reata**	July	$7.3B	CNS	Reata focuses on rare disease, including Skyclarys for Friedreich's ataxia.
Roche	**Telavant**	October	$7.1B	Immunology	Similar to Merck/Prometheus, Telavant has an asset targeting TL1A.
Astellas	**Iveric**	April	$5.9B	Ophthalmology	Iveric brings Astellas a portfolio of assets for rare retinal eye diseases.
BMS	**Mirati**	October	$4.8B (plus $1B CVR)	Oncology	Mirati has launched Krizati, for lung cancers with G12C mutations.
BMS	**RayzeBio**	December	$4.1B	Oncology	RayzeBio is developing a portfolio of radiolig and assets for various cancers.

*For this table we used a common broader definition of PM, which includes therapies that rely on various dimensions of patient stratification e.g., disease phenotype, environmental, lifestyle factors etc., rather than the narrower definition provided on page 2 of this article. Grayed entry is non-PM.

Sources: KPMG; "The top 10 biopharma M&A deals of 2023," Fierce Pharma, February 5, 2024; Cell, "Precision medicine in 2023 – seven ways to transform healthcare," March 18, 2021

Background on precision medicine

Since the milestone nearly 25 years ago of the approval of Herceptin, widely regarded as the first precision medicine, the field has evolved at a rapid pace, in large part due to our increased understanding of the underlying drivers of disease.

62 FDA-approved oncology therapies with a CDx

Currently, there are 62 FDA-approved targeted oncology therapies with a companion diagnostic (CDx)[2] on the market for a variety of cancers.

However, this has also increased the complexity in treating cancer patients. New precision medicine treatments, multidrug treatment algorithms, and advanced diagnostic and testing technologies such as liquid biopsy and next-generation sequencing have all contributed to an explosion in patient data and options that providers must navigate. This complexity is particularly burdensome for physicians in the community setting, where the vast majority of oncology patients are treated. Community physicians, unlike their peers in academic medical centers, are not specialized in one cancer type, and may not routinely follow biomarker testing guidelines or fully understand how the test results link to specific treatment options for a variety of reasons.[3] Lastly, despite holding so much promise, precision medicine can be daunting to navigate due to a multitude of new stakeholders involved in the care continuum, reimbursement issues for certain types of tests, and differences in testing approaches across countries, and sometimes even within countries.

Balancing the pressure of a competitive precision medicine deal market with the increased complexity of doing diligence on PM opportunities has significant implications for the biopharma deal team. The ability to understand complex opportunities, demonstrate being a partner of choice, and execute a deal quickly, have become critical. However, with some companies paying billions of dollars for very early-stage precision medicine assets, we believe that there needs to be some sense of "buyer beware," as the complexities of the precision medicine market have stark implications for how the deal team builds its revenue and valuation models, or even structures the deal terms.

[2] Companion diagnostics are required by the FDA label under Indications and Usage or Patient Selection.

[3] JCO Oncol Practice, "Closing the Testing Gap: Standardization of Comprehensive Biomarker Testing for Metastatic Non-Small-Cell Lung Cancer in a Large Community Oncology Practice," June 19, 2023

Complex deal assumptions

As precision medicine deals become more competitive and values continue to climb, buyers will benefit from having a more thorough approach to the financial forecast. Below we lay out key questions that can substantially impact revenue projections, costs, and the level of uncertainty within a PM-centric deal.

PM deal revenue considerations

Do we have a good understanding of the potential biomarker prevalence?

Beyond simply considering disease prevalence, deal teams must consider what percent of patients will have the relevant biomarker that the drug targets. This can become a major source of valuation uncertainty for novel or low prevalence biomarkers, where less data to inform assumptions are available. Topics that require greater scrutiny include evidence quality, and ethnic and geographic representation.

Evidence quality:

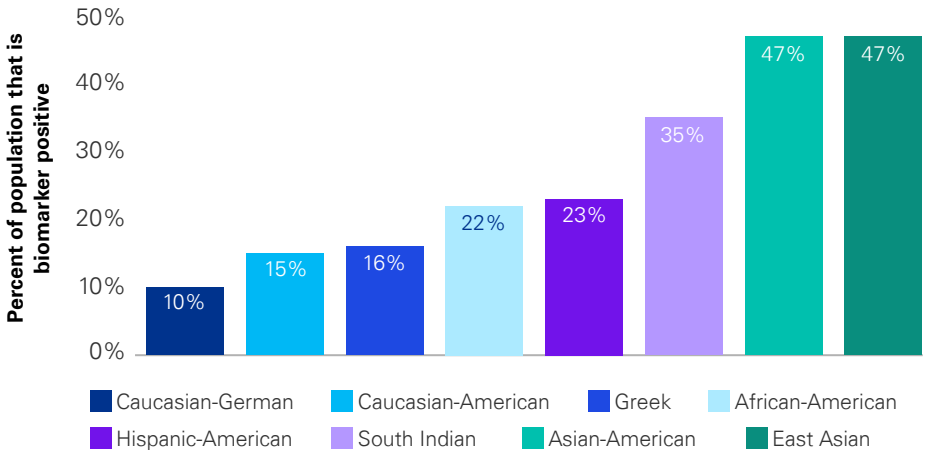
Academic studies of novel biomarkers are often in small, non-representative patient populations that may substantially overestimate or underestimate the prevalence of novel biomarkers compared to what is seen in the broader population.

Ethnic and geographic representation:

Prevalence can vary substantially between geography and/or ethnic groups (e.g., EGFR prevalence in NSCLC is ~50% among those of Asian descent versus ~13% for European)[4] (Figure 1).

Figure 1. EGFR biomarker prevalence among NSCLC patients varies significantly based on ethnic background

Only considering biomarker prevalence in one ethnic group can lead to a substantial over or under estimate of global market potential.



See chart sources on page 14

[4] Molecular Diagnostics & Therapy, "Worldwide Prevalence of Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer: A Meta-Analysis," November 23, 2021

Do we understand who can be identified as biomarker positive at launch by the technology HCPs are likely to use?

Unlike in traditional diseases where there is often a well-established definition of disease, the "biomarker positive" population can be much less certain due to not only a changing definition of what it means to be "biomarker positive" over the course of clinical development, but also limitations of commonly used biomarker tests, as well as the technology they rely on, which may limit identification of relevant patients.

Evolving definition of "biomarker positive":

- Some early-stage biomarkers are not a clear binary in terms of negativity or positivity, which introduces additional uncertainty into the forecast. To mitigate this, the deal team must consider two key questions. First, what are the potential ways that "biomarker positive" could be defined by the time of launch? Then, based on these scenarios, how do we sensitize our assumption of what percent of patients will qualify as being biomarker positive given the distribution or frequency of relevant markers in the target population?
- In a recent real-world example, we can consider the multi-gene biomarker panels used for PARP inhibitors. While initially studied in patients with any potentially relevant HRD biomarker within a small panel, in late-stage studies Akeega only demonstrated efficacy in a subset of enrolled "biomarker-positive" patients, effectively limiting the final clinically meaningful "biomarker-positive" patient population to 50 percent of the initially targeted patient population.[5, 6, 7]
- Unfortunately, data to inform assumptions on the final "clinically relevant biomarker positive" patient population is likely sparse to nonexistent for early-stage deals. However, deal teams need to be ready to develop scenarios and shape terms accordingly.

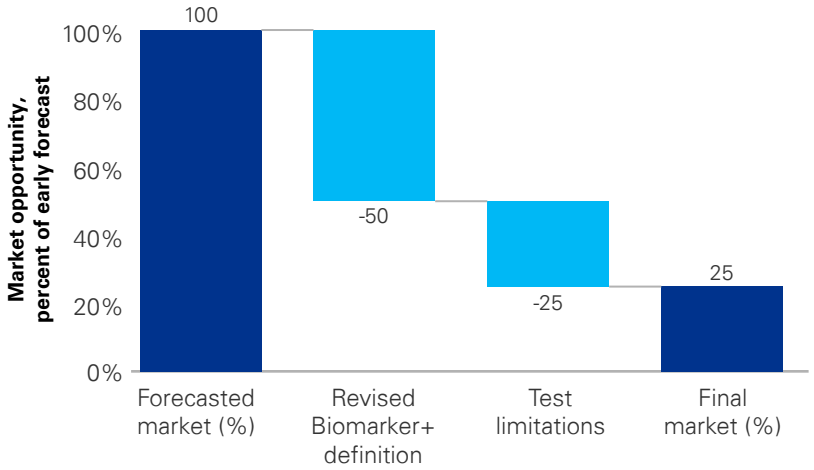
Test limitations:

Even for a well-defined biomarker, technological limitations of the diagnostic test used within a particular market may not identify all relevant patients. Depending on the level of variation, even sub-national assumptions may be required with different technologies being more commonly used in different settings of care (community versus academic) and regions within the same county (e.g., northern versus southern Italy).

- One recent example is that only ~50 percent of clinically relevant exon20 mutations in EGFR are captured by PCR technology as compared to NGS, substantially reducing the addressable market among those settings that rely on PCR test technologies.[8]

Figure 2. Hypothetical example of how an evolving definition of biomarker+ patients and test technology limitations may materially impact market potential.

Including scenario planning around the eligible biomarker+ patient population and assessment of the biomarker test technologies used in clinical practice must be conducted to avoid major potential write-downs.



See chart sources on page 14

[5] Annals of Oncology, "Niraparib plus abiraterone acetate with prednisone in patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: second interim analysis of the randomized phase III MAGNITUDE trial," September, 2023

[6] Fierce Pharma, "Johnson & Johnson's PARP combo nabs first global nod but faces tough fight against AZ, Merck's Lynparza," April 24, 2023

[7] janssenlabels.com, AKEEGA-pi.pdf

[8] "Frequency, underdiagnosis, and heterogeneity of epidermal growth factor receptor exon 20 insertion mutations using real-world genomic datasets," Molecular Oncology, February, 2023

Do we understand what percentage of patients will be successfully treated based on test results, not simply all tested patients?

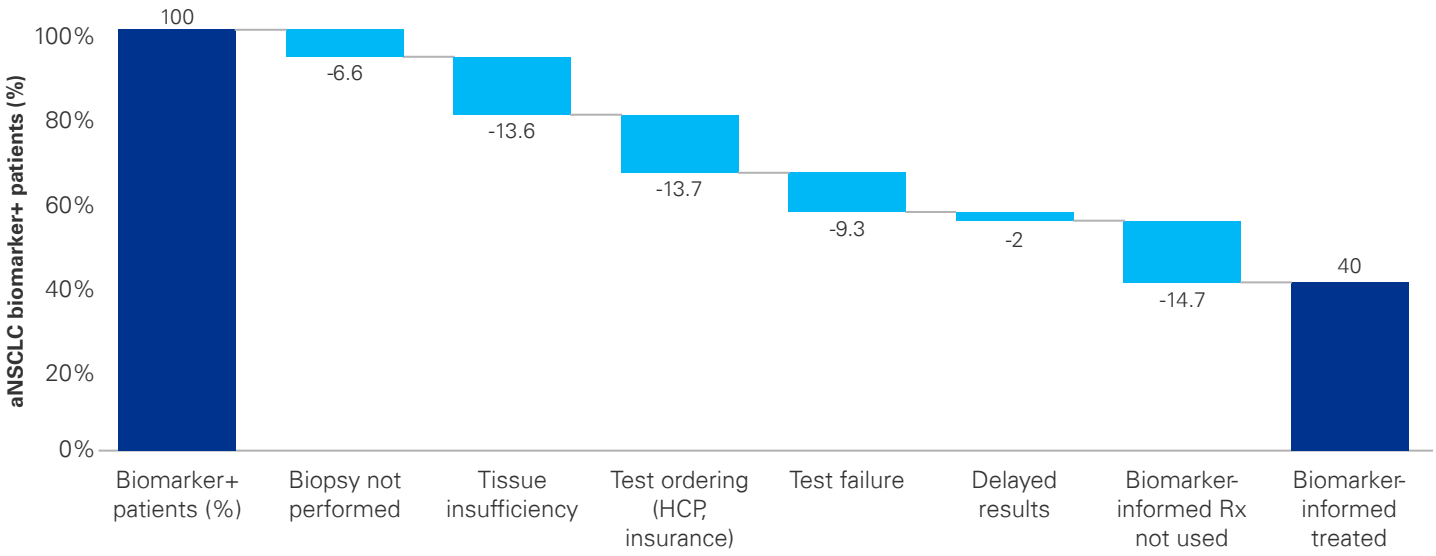
While true that "no test=no patient," deal teams who only develop testing rate assumptions may miss key risks to reaching the total addressable market. Unfortunately, the diagnostic journey is highly complex, with lack of test ordering being only one of the many potential barriers to patients receiving biomarker-informed care. For example, even in one of the most established precision medicine indications, NSCLC, recent work indicates that while the testing rate may be over 80 percent, only ~36 percent of patients receive biomarker-informed care.[9]

Patients may not receive biomarker-informed care due to:

- HCP not ordering the test, which is often where diligence teams end their analysis
- Insurance denial preventing testing
- Insufficient tissue or improperly handled tissue leading to test failure
- Laboratory error leading to inconclusive results
- Excessive test turnaround time leading providers to proceed empirically
- Lack of interpretability of the pathology report prevents appropriate therapy selection
- HCPs' lack of awareness of therapy options relevant to a patient based on reported biomarker status
- Individual treatment preferences by institutions or HCPs related to factors like operational setup, financial incentive, or personal experience with routinely used therapies

Figure 3. Patient loss across the testing journey–U.S. advanced NSCLC (aNSCLC) example

A substantial volume of patients are lost along their testing journey, necessitating deal teams to consider not just a testing rate, but the percent of patients successfully receiving biomarker-informed care.



See chart sources on page 14

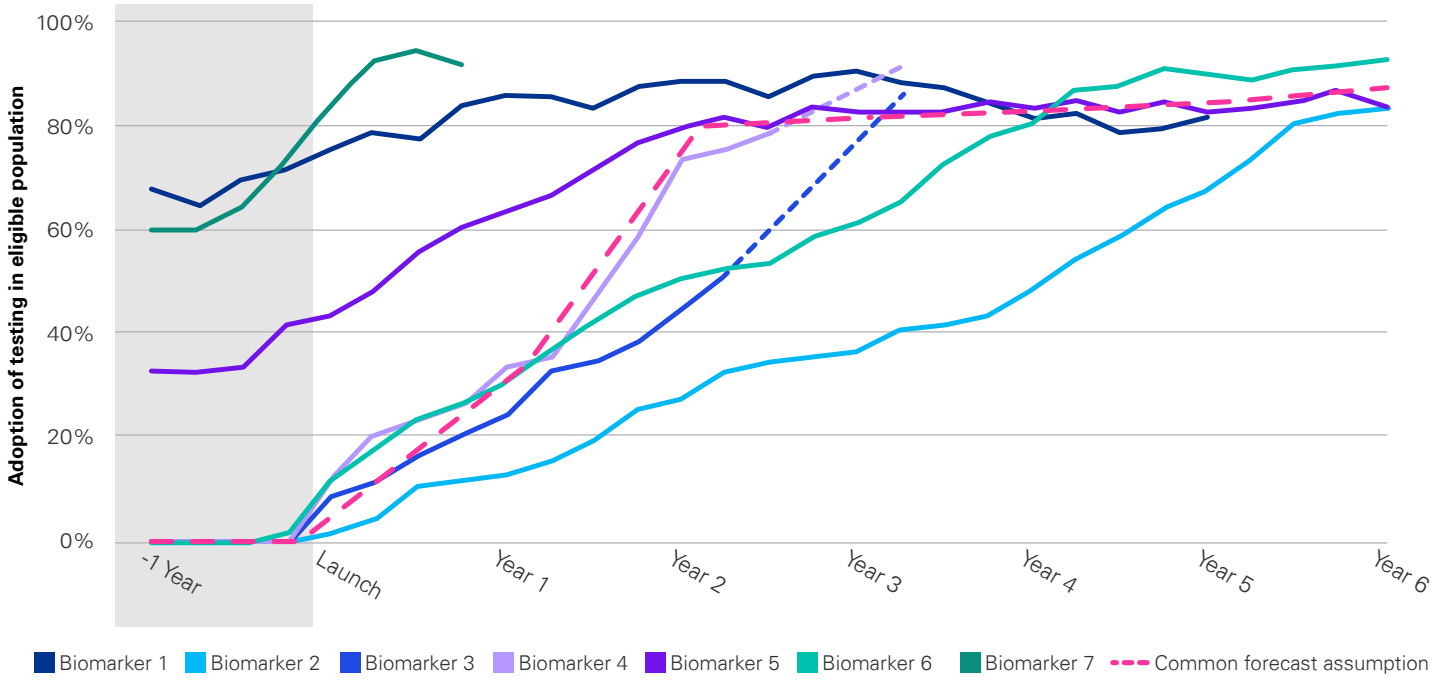
[9] JCO Precision Oncology, "Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non-Small-Cell Lung Cancer," October 31, 2022

Do we understand the testing ecosystem and how it may impact future testing?

Uptake curves for testing rates are another critical forecasting component that deserve attention. Test technology, market infrastructure, and perceived clinical utility all play important roles in shaping test uptake, leading to substantial variation in test adoption. Deal teams often use optimistic assumptions to reach high peak testing rates within a few years, without any supporting analogues or data. However, in deals that involve diseases with novel or less established testing, this approach will lead to significant overestimation on how quickly the addressable population, and therefore the peak revenues, can be reached. With the testing market constantly evolving, this demands that deal teams not simply examine "where is the market today," but "where is this market going" and "what level of investment is their organization willing to commit to drive test uptake?"

Figure 4. Testing adoption curves for common biomarker tests versus an optimistic deal assumption

Use of optimistic testing uptake assumptions warrants a more thoughtful and data-driven approach.



Dashed lines are projections

See chart sources on page 14

Why this matters....

Clearly, the deal team must be realistic when building assumptions around the addressable market, testing landscape, and points of patient loss. Without careful consideration of these factors, there are obvious risks to the top-line assumptions, with significant downstream impact on the valuation.

Additional investments are required

Beyond risks to revenue potential, successful launch of PM assets often requires additional skills and investment that must be considered in the diligence. This is driven by the fact that the precision medicine GTM model is fundamentally different from the traditional pharma model. Successfully launching a PM asset may involve spending years pre-launch shaping the market, hiring or upskilling talent, engaging new stakeholders (e.g., pathologists, genetic counselors), and building new partnerships. Thus, evaluating potential asset-driven costs and expenses for the acquirer to fill PM-related capability gaps are important considerations for validating the deal thesis.

Asset-specific considerations

What diagnostic test development has been done, and what incremental effort will be needed?

If "no test=no patient=no revenue," then evaluating the diagnostic development plan and any existing partner becomes as critical as evaluation of the therapy/asset. Deal teams must be prepared to think through the risks any existing partner poses, if more than one diagnostic may be required, and the subsequent cost implications.

- Does the currently proposed diagnostic technology work for all priority markets, or will other solutions be needed to support testing in some markets?
- How novel is the diagnostic? What level of risk and financial investment does commercialization entail?
- If there are multiple indications, could multiple diagnostic tests be required?

If the target already has a diagnostic partner, additional questions are required:

- Are their geographic scope, and regulatory and commercial capabilities sufficient?
- Do they have a track record of developing and launching tests?
- How financially stable are they?
- What is the deal structure?
- Are IP rights secured?
- How are the financial terms defined, and who holds which responsibilities?

If current testing rates are low (or a test is not currently used clinically), are we willing to invest in market shaping to reach our aggressive testing assumptions?

As discussed in our section on the testing ecosystem, launch testing rate assumptions and uptake curves are often aggressive compared to existing practice. If this is required to support the deal thesis, then the valuation must account for a robust budget to shape the testing ecosystem. Potential cost drivers to consider include:

- Educating providers on the need to test, when to test, and how to interpret results
- Ensuring laboratories adopt the test and can successfully run the test
- Engaging other precision medicine ecosystem stakeholders (e.g., genetic counselors) to support testing awareness and adoption
- Addressing testing access barriers

Acquirer capability gaps

Does our R&D team have the necessary experience in the relevant TAs to ensure successful diagnostic decision-making and co-commercialization when warranted?

A successful R&D program for PM assets must go beyond just the development of the actual drug. Determining what type of diagnostic will be needed and addressing partnership management are critical to ensure timely and cost-efficient diagnostic development and approval, where required. While some organizations have experience in driving such programs within oncology, as PM expands to other therapy areas and diagnostic technologies (e.g., imaging, AI algorithms), pharma capabilities are less established. Diligence teams must ask themselves if their organization is willing and capable of making the necessary investments across multiple dimensions (e.g., people, process, and technologies). If not, PTRS (probability of technical and regulatory success) will underperform assumptions made based purely on drug class and therapeutic area.

Do we have the local talent to maximize commercial value in priority markets?

From a geographical perspective, precision medicine is highly heterogeneous. The level of centralization of testing, the available test technology, and testing stakeholders all vary by geographic market, with even substantial variation within some countries. Reimbursement is another highly disparate factor to consider, with some markets requiring pharma-sponsored pay for testing programs. In short, PM brings in a level of complexity that must be understood on a country-by-country basis to be successful. Bringing in the right talent that can navigate these complexities is essential, but this comes at a cost because this talent can be scarce and expensive.

Does our existing PM talent engage the needed ecosystem stakeholders to support the TA?

Just as there are unique PM dynamics across geographies, the same is true across therapeutic areas. Thus, companies must also consider that there may be fewer synergies than they anticipate with the TA/portfolio, even if the company operates in the specific TA. For example, existing precision medicine field teams supporting engagement with oncology testing labs will not be able to easily expand to support testing for an inherited rare disease asset. Testing in each space is often done by different labs, requiring building of new relationships, and targeting different facilities, all of which have implications to projecting commercialization costs.

Conclusion

In summation, the diligence of PM assets is fundamentally different from "traditional" non-PM assets. The complexities outlined in this paper highlight why the diligence team must ensure that there are representatives at the deal table from the appropriate PM teams across both R&D and commercial with expertise spanning priority markets. Too often, we see teams not bringing the right internal stakeholders to the diligence table, leading to groupthink, poorly informed decisions, inflated valuations—and future write-downs.

How KPMG can help

The Precision Medicine deal market is one of the most active and dynamic in the Life Sciences industry. Our Precision Medicine team provides clients with end-to-end deal support, from deal strategy, target identification and prioritization, commercial, financial and operational diligence, to execution for acquisitions, mergers, and divestitures and post-deal value capture. Our practice has been on the buy- and sell-side for deals in the Precision Medicine ecosystem for both corporate and private entities.

To learn more about our Precision Medicine practice click below:

KPMG in Precision Medicine

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Alasdair is a leader in the KPMG Precision Medicine practice. He has over 20 years' experience in strategy consulting specializing in inorganic growth and commercial strategy and portfolio optimization for biopharmaceutical, genomic, diagnostic, and health system clients, as well as private investors. He has worked on numerous buy-side precision medicine deals for both corporate and private investors across the oncology diagnostics and cell and gene markets.

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As the Life Sciences Sector and Global Healthcare and Life Sciences Deal Advisory and Strategy Leader at KPMG, Kristin has been working in the healthcare and life sciences markets for almost 30 years. She leads the full continuum of complex transaction support, from growth and corporate strategy to multidisciplined diligence to integrations and divestitures of healthcare and life sciences companies and divisions, from the most innovative companies to the most entangled basic businesses in pharma, device, lab, tools, and diagnostics on a global scale. She works with both private equity and corporates on the most complex and varied global precision medicine deals. She is also an author, a producer, and a speaker in the life sciences space. Her book, Personalizing Precision Medicine, garnered attention worldwide for its all-inclusive and comprehensive look at global precision medicine. Kristin's specialty is complex scientific and clinical transactions, providing a holistic lens, typically crafting the overall strategy for the deal and the company/entity, moving her teams into diligence, then into the execution of the deal and the performance transformation as a result either for the new entity or the RemainCo.

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Jason is a member of the KPMG Precision Medicine practice. He has over 8 years of experience in life-sciences strategy consulting, spanning commercial diligence, process improvement, portfolio optimization, launch planning, and organizational design. He has worked across both buy- and sell-side deal work, with a focus on early-stage oncology assets and life sciences R&D platform technologies.

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Chart sources

Figure 1

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Cancer Science, "Comprehensive genomic profiling of lung cancer using a validated panel to explore therapeutic targets in East Asian patients," December, 2017

Figure 2

Revised biomarker definition modeled after Akeega and related references cited elsewhere. Test technology limitations are modeled after PCR missing exon20i patients and related references cited elsewhere.

Note: Here we assume a worst-case scenario where all patients were tested with PCR for illustrative purposes. However, we acknowledge this does not reflect current clinical practice in the U.S.

Figure 3

Source: JCO Precision Oncology, "Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non-Small-Cell Lung Cancer," October, 2022

Notes: This illustrative waterfall is based on U.S. data for NSCLC, which is likely to under-estimate patient loss in most other indications or geographies where testing is less well established. Final biomarker-informed treated patients in the figure is higher than in the cited publication due to excluding patient loss from test sensitivity, as that issue was discussed in the prior section.

Figure 4

Blinded proprietary data, Diaceutics PLC

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