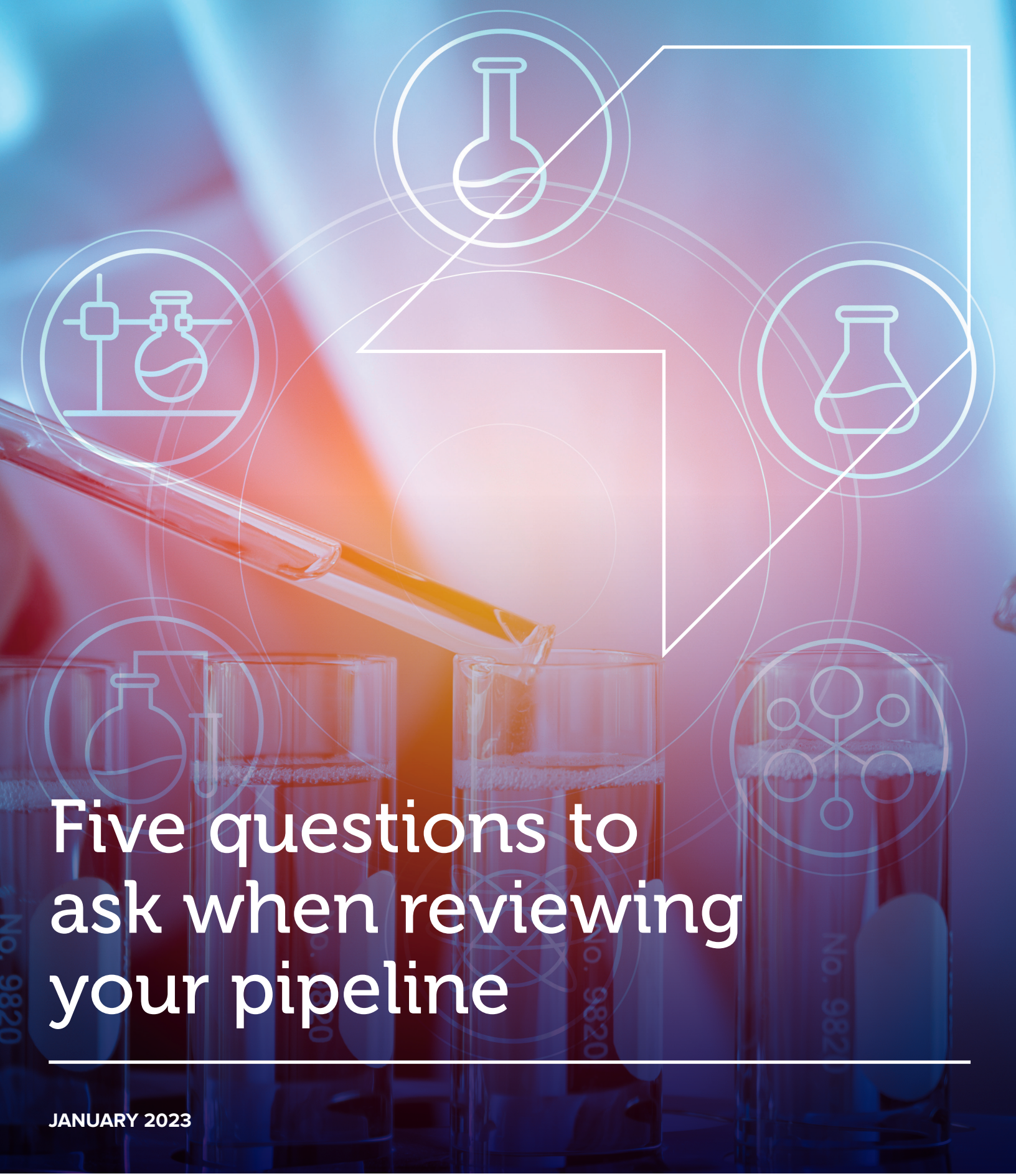

Five questions to ask when reviewing your pipeline

JANUARY 2023

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Pharma's R&D pipeline is its lifeblood. The industry-wide pipeline is today worth a staggering $1.4 trillion, according to **Evaluate's Omnium**. Yet, at the company level, it can be very difficult to get R&D priorities right. Decade-long development timelines, new technologies, regulatory hurdles, an ever-changing competitive landscape and budget-conscious payers all need to be taken into account when building and maintaining a healthy pipeline.

As science and policy evolve, most of these variables are becoming less, not more, predictable. New drug modalities, for example, require fresh regulatory pathways and may present unexpected commercial challenges. New tools, like artificial intelligence and wearables, can help cut costs,

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but also require different workflows. New laws, such as the US Inflation Reduction Act (IRA), introduce additional strategic considerations whose full consequences are **years from being fully understood.**

There is no template to follow in pipeline planning, and few short-cuts. But whatever your area of expertise, here are five questions you should be asking when building or reviewing a pipeline.

1. Do you really understand how your product is differentiated?

If your target product isn't clearly differentiated from what's already out there, no one will buy it. It's unwise to make an investment or prioritisation decision before properly understanding those potential advantages.

Why would patients want and need your drug, why would a doctor seek to prescribe it, and why would a payer reimburse it? If you're first-to-market in a given therapy area, the answer may be straightforward. But if you're launching into a competitive space, it's important to be clear about your value story, whether that's about better efficacy, safety, convenience – or simply lower cost.

How to get it right: Regular scenario-building. Scenario building is a powerful way to capture how your product might be positioned. Using partial or early data can allow exploration of different hypotheses, including best- and worst-case. These scenarios should be run regularly: standard-of-care may change. A competitor might introduce a new product. Refining your assumptions to take into account potential or actual change provides deeper insight and may inform adjustments to the R&D program or to regulatory and commercial planning.

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2. Are you keeping track of new market entrants?

Failing to track new market entrants or disruptors is a common pitfall in pipeline prioritisation.

Competition is constantly evolving, as are standards of care across every sector of the market. Be sure to check beyond the immediate treatment group or drug class to other categories of care that may impact your market – how a digital therapeutic might impact the treatment of some psychiatric conditions, say, or how generics in an adjacent space may have a knock-on effect on pricing in your own area.

Look beyond the press releases, company announcements and industry conferences covering your competitors' developments; consider what their strategies may be. Put yourself in their shoes: what would you do? Also be aware of the impact of M&A or wider business development on market dynamics. If your competitor is bought by a larger player before you get to market, how might that impact your own launch?

How to get it right: Applying pipeline data and predictive metrics to examine market evolution is a powerful tool in planning for the unexpected – and the expected. Brainstorm and test different scenarios, including how treatment paradigms may change, and/or pricing dynamics evolve. Which, if any, of these scenarios might change your investment strategy?

Consider your competitors' experience, too, in deciding what to prioritise. What can you learn from the trajectory of other market entrants? Are you likely to face similar headwinds or tailwinds?

3. Is your target population forecast realistic?

It's easy to misjudge the addressable patient population for your drug. Have you got the right trial design to gain approval for all the patients you hope to help? Have you taken into account treatment history, disease severity and the most important endpoints – both for regulators and for patients and their physicians? Regulator-recognised endpoints are important for approval, of course, but patient-reported outcomes and other measures of symptom relief, plus avoidance of costly complications, may be even more crucial to patients, prescribers and to payers in deciding whether to reimburse the product. These can make the difference between commercial success and failure, particularly in crowded therapy areas.

Target market size can – and often does – change. Your product might be approved initially in a small segment of patients and broaden out as experience and data build. Your development plan will reflect this possible evolution.

But misjudging your target market in either direction can be damaging – especially prior to first launch. Aim too high and you risk disappointing the market and your investors. Too low, and you undersell the program, potentially scuppering deal-making and further financing opportunities.

How to get it right: Effective modelling is critical in understanding your market size and potential. Make sure that you have detailed epidemiology and patient segmentation data so you can forecast effectively. Explore a range of scenarios, just as for your product differentiation and competitive landscape analysis. What is the narrowest patient population? What might be the broadest? What if the product sits somewhere in the middle? Consider, too, how your product's early positioning and labelling may impact not only its uptake, but also that of fast-following competitor products.

4. Are you ignoring payers and market access in early portfolio decisions?

If you are focusing only on the science, then stop and think again. Your new drug may be the clinical equivalent of the best thing since sliced bread, but make sure its price is in line with the outcomes it can deliver to patients. Every healthcare system in the world – even the US – uses some form of cost-benefit analysis. Make sure your value story is backed up with robust health economic data, and be willing to consider value-based reimbursement arrangements, especially if you're coming to market with a high-priced gene/cell therapy, or a novel mechanism in a therapy area that's dominated by cheaper generics.

By and large, fair pricing from the outset can pay off with faster access and higher volumes. But the US Inflation Reduction Act may encourage higher launch prices as it imposes curbs on annual price increases. It will also subject the costliest Medicare drugs to price negotiations from 2026. Price negotiations will affect only a handful of drugs initially. Newer products – small molecules on the market for fewer than 9 years, or biologics younger than 13 – are protected. So are those with generic competition, or orphans with a single approved indication. *(See box on page 6: Inflation Reduction Act kicks off US drug price negotiations.)*

The law may have several implications. It might dis-incentivise development of small molecules, for instance, given the shorter exclusivity period, or steer developers away from diseases that cost Medicare most dearly. It might deter developers from pursuing multiple indications for an orphan drug.

The full picture has yet to emerge. But although the IRA is a significant new factor to bear in mind when reviewing or planning a pipeline, its effects should not be overblown.

Medicare is just one payer – albeit a big one. It's important to remember that not all payers are alike. Their priorities are different, just as their covered populations are. Market access analyses must consider the needs and touchpoints of each type of payer – whether it's a national health system in Europe, or, in the US, an accountable care organisation, a PBM or Medicare. Understanding each system is important and applying learnings to pipeline development decisions at the earliest stages can prevent painful and expensive setbacks down the line.

How to get it right: Make sure you're **factoring in payer perspectives** as early in the pipeline as possible. You'll revisit your assumptions as the market evolves, and as your own asset matures, but leaving it until you're ready to build your go-to-market strategy is never wise. Understanding what payers are looking for in a new drug will give you a much better chance of commercial success.

5. Do you have an overly rosy view of your product candidates?

Of course you do. We all seek confirmatory data to support our existing opinions (or drug candidates) and ignore contradictory evidence. Try to work against that natural bias. Clear eyes are necessary to make sure you're taking the right drugs in your pipeline forward at the right time. Ensure your assumptions are as objective and considered as possible; seek out opposing viewpoints and nay-sayers to test those assumptions.

Failure to do so could lead to expensive mistakes, be it a potential blockbuster languishing in the pipeline or progressing a product that doesn't make the mark. Most drug launches under-perform, and the time to peak sales has slowed over the last decade or two. This reflects both a more challenging reimbursement environment, but also over-optimistic forecasts.

How to get it right: Include data-driven evidence in your planning process and source external data and viewpoints. It may sound obvious, but incorporating benchmarks and other contextual data, along with external expert opinion is critical. You might want someone to tell you that your baby is beautiful, but if that's not the case, you need to know.

Conclusion: learn from competitors' experience and make use of available data and analytics tools

Overall, in pipeline planning, there's always much more to learn from competitors' experiences than we want to believe. Granted, science is progressing fast, and more players may have a first-in-class modality or represent the first effective treatment for a given condition. But in most cases, there is a story to learn from – whether it's the most recent market entrant, similar dynamics in an adjacent therapy area, or a creative market access approach in an entirely different space, or even sector.

Seek out those stories. And make best use of the extensive data and analytics tools available, often with easy-to-use graphic interfaces that allow clear visualisation of the impact of different decisions and external/competitive dynamics. Building up the most comprehensive, objective view of your pipeline prospects will help build the best portfolio, generate the most valuable products for patients, and help drive the pharma industry's **strong growth over the coming decade**.

Inflation Reduction Act kicks off US drug price negotiations

The Inflation Reduction Act, signed into US law in August 2022, charts a path to price negotiations for some of the highest-cost Medicare drugs, and, from 2023, curbs annual above-inflation price increases for all Medicare treatments. It's expected to save the government $100 billion over ten years and has provoked strong pushback from industry, which says the Act will dampen innovation and reduce the number of drugs in development.

Yet the IRA will not curb prices on all pharmaceuticals, as is typical in European and other nations. Negotiations will apply only to the highest-cost small molecules, with no generic competition, which have been on the market for at least 9 years. Negotiation-eligible biologics must be at least 13 years from approval and have no biosimilar counterparts. (Selection for negotiation may start after seven and 11 years respectively.) The first ten Part D (outpatient) drugs will be negotiated in 2026, with numbers ratcheting up in subsequent years. Hospital-administered Part B drug price negotiations start from 2028.

It didn't take long for industry to blame the IRA for pipeline prioritisation decisions, and for unintended consequences of the Act to emerge. A particular concern for industry is the discrepancy between the grace period for small molecules and that for biologics, which they claim will dis-incentivise manufacturers from developing small molecules. Novartis has already said the commercial potential of its small-interfering RNA cholesterol drug Leqvio may be impacted. Alnylam has delayed development of a second indication for its rare disease treatment Amvuttra, since single-indication orphan drugs are exempt from negotiations.

Limiting the number of indications for some orphan drugs is one unintended consequence of the Act. Another is near-term increases in some list prices as companies seek to compensate for lower-than-hoped annual rises down the line. (Penalties for flouting the inflation curb or price negotiation rules are harsh.) A third consequence may be innovator-biosimilar deals seeking to game part of the law that allows biologic price negotiations to be delayed for up to two years if biosimilar competition is expected.

There's some posturing going on, as industry seeks to add weight to legal challenges facing the IRA – challenges that may accelerate after Republican gains in Congress in the November 2022 mid-terms. But IRA isn't going away: neither party wants to be seen favouring industry over patient access to medicines, and there are other parts of the Act, like a $2000 annual cap on out-of-pocket costs for Medicare patients, that voters wouldn't want to lose.

Still, plenty of questions remain. It's possible, likely even, that some provisions of the Act will look rather different in 2026 and beyond than they do today. IRA is another factor for companies to consider in their pipeline prioritisation decisions - **one whose full face has yet to be revealed.**

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