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Preparing for the new wave of innovation:

BioPharma Operating Models amidst the growth of new modalities

Introduction

The moment that 90-year-old Margaret Keenan became the first person to receive a COVID-19 vaccine in December 2020 was hailed around the world, marking the beginning of the end of the pandemic.[1] However, the pace of developments in BioPharma across the last decade mean that with the passage of time historians may look upon Margaret's jab more prosaically, considering mRNA vaccines as just one of a number of modalities that will transform outcomes for patients.

These new modalities are beginning to reach patients with consequence in a number of areas, whether in the use of curative Gene Therapies for Haemophilia A like BioMarin's Roctavian (Approved in 2022),[2] Alnylam's siRNA drug Patisiran (Approved in 2018),[3] or Novartis' CAR-T Kymriah (Approved in 2017),[4] or others including CRISPR based Gene Editing, ADCs and Bispecifics. At the same time, the Inflation Reduction Act will decrease the potential lifecycle revenue of many products, adding impetus to more rapid development of new products to fill revenue gaps. Amidst this backdrop, BioPharma companies are rethinking how they structure their organisations, positioning themselves ready to put these breakthrough modalities to wider use, whether through commercialising themselves, collaborating with others or specialising in key aspects of the BioPharma value chain.

BioPharma companies are already responding to this new wave of innovation by:

- **Shifting investment focus to a new wave of modalities,** that can cater to unmet needs. BioPharma companies are investing in a new generation of modalities including Bispecifics, RNA Interference and Gene Editing, typified by deals like Sanofi's $3.2B acquisition of mRNA therapeutics specialist Translate Bio in 2021[5] or Novo Nordisk's 2021 partnership with Heartseed in Cell Therapy for Heart Failure.[6] This shift is reflected in FDA approvals of new biologics overtaking small molecules in 2022, with new biologic modalities like Bispecifics and Gene Therapies accounting for half of biologic approvals, in spite of the challenges in developing and producing these products.[7]

- **Striking partnerships** around next generation platforms. Daiichi Sankyo's Antibody-Drug Conjugate (ADC) focused partnership with AstraZeneca[8] and CRISPR Therapeutics' Gene Editing partnership with Vertex[9] typify the approach some BioPharma companies are taking. These agreements enable the smaller partner to validate research and extend their R&D funding, whilst accessing the commercial footprint and expertise of larger players. In Daiichi's case, their relationship with AstraZeneca helped them to launch Enhertu faster and more effectively, gaining access to a partner with mature commercial and development capabilities in Oncology.[10]

- **Divesting lower-margin product lines**, specialising in fewer, niche areas. Large-cap BioPharma companies including GSK (Haleon) and Novartis (Sandoz) have divested key assets as part of attempts to focus their business models on higher margin products in key therapy areas. Novartis CEO Vas Narasimhan cited the ambition of *'building a focused innovative medicines company'*[11] as the driver behind the Sandoz separation, reflecting the preference of large BioPharma companies towards focusing on novel modalities.

- **Utilising a wider ecosystem of partners** across the product development cycle. Established BioPharma companies are using 3rd party specialists to access niche capabilities to discover new products or develop more holistic solutions for patients. Beyond the wider use of AI partnerships to support R&D and back office functions across the industry, sequencing provider Illumina has agreed a range of partnerships in Oncology to develop companion diagnostics for new treatments,[12] whilst UCB agreed a collaboration with BrightInsight in 2022, to develop a digital disease management solution to support patients with Myasthenia Gravis.[13]

- **Navigating a challenging pricing landscape**, amidst budget pressure in the US and Europe. The Inflation Reduction Act in the US will constrain both the pricing freedom and lifecycle potential of many assets, particularly small molecule drugs,[14] whilst proposed EU reforms could limit the length of exclusivity for new medicines unless they adhere to conditions including running head-to-head trials.[15] Key markets including Germany and the UK have introduced reforms designed to constrain prices including increased mandatory rebates and restrictions on free pricing, reflecting the systemic challenges to healthcare budgets driven by ageing populations and macroeconomic stagflation.[16]

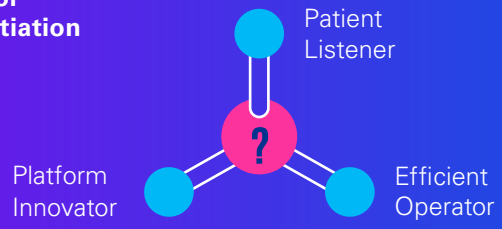
BioPharma companies are moving towards three distinct ways of orientating their businesses to provide value to partners, patients and payers

Amidst this shifting landscape, BioPharma companies are increasingly orientating around more distinct sources of differentiation. We outline three archetypes that we believe will represent how BioPharma companies choose to orientate both their Business and Operating Models:

Exploring the next generation BioPharma archetypes

Archetype	Patient Listener	Platform Innovator	Efficient Operator
Point of Differentiation	Competitive advantage orientates around deeper penetration in targeted disease areas, differentiating themselves through orchestrating diagnosis, treatment and post care, personalising care to ensure greater take-up amongst patients.	Innovation drives competitive advantage, through development of novel multi-purpose modalities agnostic of disease targets, driven by both in-house R&D and networks of external partners and academic collaborations.	Competitive advantage is rooted in being faster, cheaper and more seamless at bringing products to patients, enabled by greater efficiency in scalable and repeatable activities across the BioPharma value chain, derived from scale, superior technology or more effective ways of working.

Source of Differentiation



$230 billion

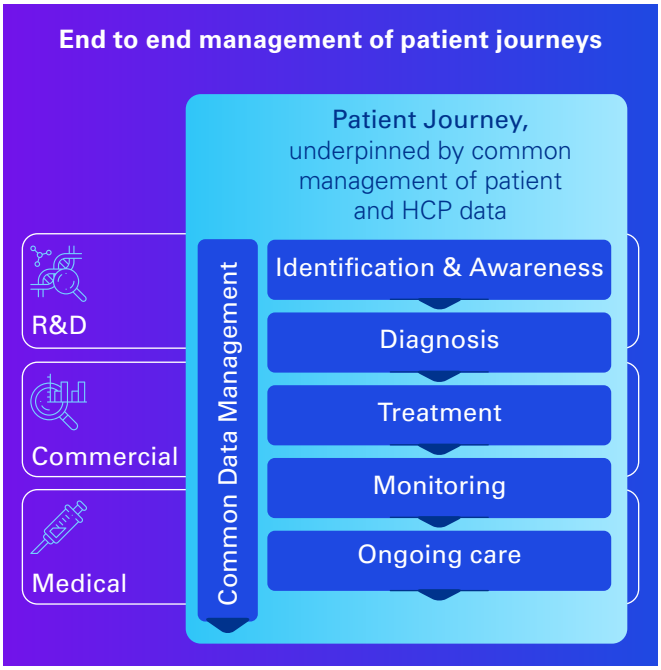
in sales could be at risk between now and 2030, as almost 200 drugs lose patent protection[17]

The Patient Listener

Patient Listeners centre the patient journey as the 'north star' to which product development and commercialisation is tied. The organisation is structured around select therapy areas or markets with specialised approaches to reaching patients in each. Clinical data and feedback from HCPs & Patients, from early-stage trials to real-world evidence collection is the lifeblood of a Patient Listener. This data becomes a source of continuous learning, whether in identifying how off-target effects can be prevented, or by understanding how to track the endpoints that are most likely to evidence the game-changing potential of a new therapy. When most effective, Patient Listeners cut across typical boundaries to integrate offerings like telemedicine, diagnostics, and disease management, presenting patients with precision medicine solutions, tailored to their needs.

Patient Listeners grow by using an intimate understanding of their patients and healthcare systems to adopt a precision medicine approach

Patient Listeners work across functions to develop and commercialise products with a singular focus on breaking down the barriers to positive patient outcomes. Novartis' *'US-first'* strategy typifies this approach, with the ambition to reduce the *'frictions'* that are common across therapeutic areas, *'including daunting prior authorization requirements and co-pay burdens on patients'*,[18] which has led to geography as a key dimension of their Operating Model. Others are leading the way in creating cross-functional capabilities that enhance patient centricity. UCB cite decentralised clinical trials as key in reaching underrepresented populations in development stage, in turn getting a more representative sample of patients.[19] Roche's precision medicine approach cuts across typical functions, from proactively improving access to biomarker tests for patients, to utilising advanced analytics on the prevalence of biomarkers to guide future R&D targets.[20]



Consumer genomics provider 23andMe are even developing their own immune-oncology asset, utilising their vast data sets to understand and target the root causes of diseases,[21] transcending normal sector boundaries and reflecting the increasing importance of exploiting omics data as an asset for Patient Listeners.

Patient Listeners need to foster interfaces between functional teams across the lifecycle as part of their Operating Model

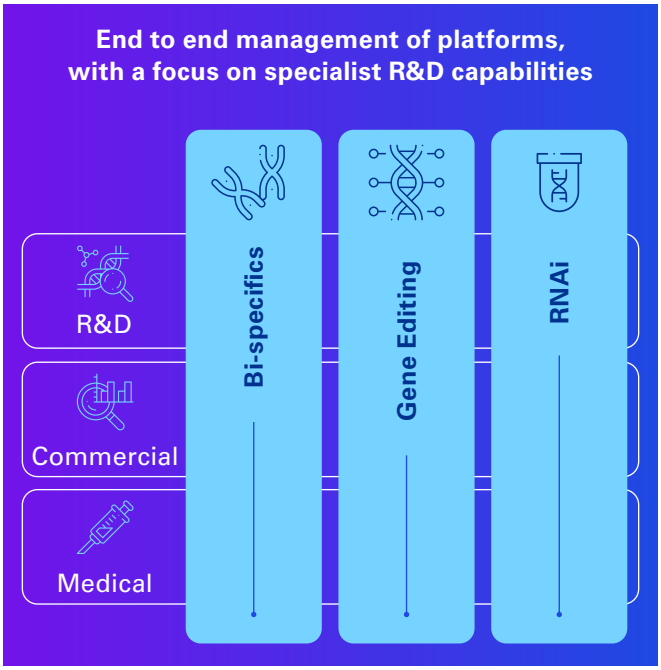
Success for Patient Listeners means being able to apply their understanding of what patients need, across the development and commercialisation process, ensuring that this is reflected in aspects like clinical trial design and availability of biomarker testing. As much as this necessitates a common data warehouse, drawing inputs from different functions across the development lifecycle, a dedicated data strategy is vital for Patient Listeners, understanding what types of data can be collected from patients or HCPs as part of the organisation's touchpoints with them.

The Platform Innovator

Platform Innovators design their organisation around modalities or platform types, typically focusing on developing new modalities to clinical stage and beyond. Platform units can work autonomously with potential partners to accelerate development. Research, manufacturing, and potentially even commercial activities can be aligned to each platform unit, though enabling activities like supply chain and corporate functions may be shared across platform units. Whilst smaller players will focus on different utilities of a single platform, larger players are most effective when incubating various new technologies to commercial stage.

Platform Innovators can accelerate growth, through greater speed and agility in research and development

Decisions around how to structure R&D activities are the critical focus for Platform Innovators. For emerging BioPharma companies without revenue streams, managing multi-purpose technologies in terms of the potential uses in different therapy areas allows them to share or sell rights to some programmes, concentrating resources on the most promising disease targets or accessing the investment needed to initiate further clinical studies. As BioPharma companies become established, being a Platform Innovator assumes a different meaning, with emphasis on continually developing untested modalities to commercial stage. To do this, established players must seek to replicate the agility of Biotech, able to pivot quickly, unburdened by the deliberative decision-making that typically arises in large public companies, and offer a compelling proposition to attract potential partners. Bayer launched a CGT focused *'Co.Lab'* in Boston in May 2023, building on bases in Berlin and Japan designed to act as incubators for early-stage partners.[22] Similarly, Sanofi established an mRNA centre of Excellence with ring-fenced funding of €400m a year, in tandem with their acquisition of TranslateBio in 2021, to accelerate development of a new generation of vaccines.[23]



The capability to incubate and develop new modalities with others is crucial for a Platform Innovator

For larger BioPharma companies, being a Platform Innovator means going further than a portfolio investor, providing partners with value beyond funding alone. This puts a premium on flexibility, to offer potential partners support that fits their needs, whether through guidance on clinical trials or support in establishing manufacturing capacity. This willingness to collaborate needs to be ingrained across the organisation for larger BioPharma companies, whether through commercial leads co-developing pricing policy or development teams enabling seamless sharing of clinical data during trials.

65%

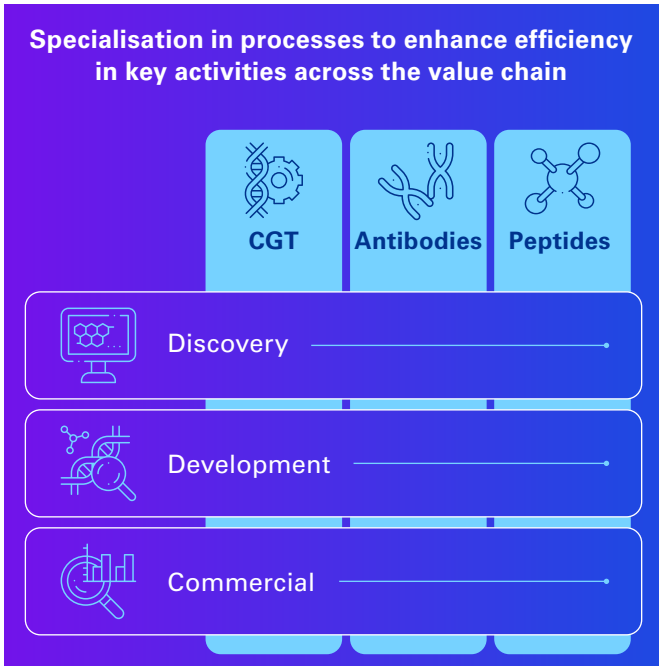
of BioPharma executives said they thought 2023 would be charactered by a high number of strategic partnerships, more than any other deal type[24]

The Efficient Operator

Efficient Operators typically focus on product categories or processes that provide an anchor for their organisation. They will seek to reduce or minimise the risks inherent for BioPharma companies through concentrating on scalable activities or focusing on niche services and markets. They may centralise functions or centres of excellence to act as drivers of improved productivity in processes like manufacturing, or develop scalable commercial capabilities to bring new treatments to market more efficiently than their peers.

Efficient Operators can accelerate growth through improving productivity in critical activities across their value chain

Efficient Operators can deploy differential capabilities in crucial aspects of the BioPharma value chain for both existing and new modalities. Dr Reddy, the Indian-based Pharma known best for generic manufacturing, outlined their *'Horizon 2'* strategy, identifying areas including Biosimilars and Biologic manufacturing as growth areas where scale and technological advantage can be leveraged.[25] Similarly, German-based Evotec has developed a differentiated business model to many CROs, offering both services like drug discovery and regulatory affairs support, and progressing products beyond discovery stage with the aim of agreeing partnerships with large BioPharma companies that de-risk development efforts.[26] Efficient Operators will defy the typical boundaries between BioPharma, CDMO and CROs to become specialists in key processes, using this strength to offer differential services that drastically improve traditional ways of doing things, and potentially enable them to bring products to market independently. AI modelling specialists Evozyne typify the increasingly sophisticated expertise industry leaders are looking to draw upon, collaborating with NVIDIA on deep learning models to support protein design for BioPharma companies.[27]



The capacity for continual improvement needs to be built into the Operating Models of Efficient Operators

Given the pace of innovation in BioPharma, Efficient Operators need to be more than simple service providers. Creating the space for continued development of capability is fundamental, whether it is through dedicated teams committed to the development of new technology, or by introducing a '20% rule' to give staff time to launch experimental projects in line with day-to-day responsibilities.

32%

of BioPharma executives felt Biosimilar targets have become more attractive because of the impact of IRA[28]

What does Operating Model change entail for BioPharma companies?

- **Aligning around which next generation archetype is most suitable is a prerequisite for change**

With multiple archetypes in play, it is tempting for BioPharma companies to declare that they want the best of all worlds and design a hybrid Operating Model. However, small or mid-sized BioPharma companies are likely to have a primary source of differentiation but may fail to identify and align on what this is. This often reflects diverse senior executive perspectives around sources of growth and competitive advantage – this misalignment can lead to increased people and infrastructure costs that become difficult to unlock as the company scales. A BioPharma client we observed found that failing to clearly define which archetype best fit made it challenging to identify the priority areas for capital allocation and investment, e.g. new asset acquisition, launch and/or new technology platforms. This created conflicts and delays in setting the annual organisation budget and hindered decision-making as there were few cross functional forums established.

BioPharma companies should identify which archetype is most suitable through an internal and external lens: internally, by evaluating their core competencies since inception, and externally through insight on patient, payer and/or partner requirements. Otherwise, they risk finding themselves with a half-baked Operating Model design that caters to multiple sources of differentiation – leading to unclear accountabilities, ill-defined roles and confused decision-making.

- **Different business units can be based around different archetypes**

Although small to mid-size BioPharma companies may orient around a single archetype, as they grow larger BioPharma companies may deploy multiple archetypes with different business units orientated around specific sources of competitive differentiation. Both the positioning and maturity of an organisation's portfolio and target markets will shape this. In new, competitive markets like GLP-1s in Obesity, first to market players have thrived by developing products with patient needs in mind but may need to pivot to a focus on operational efficiency to compete amidst growing competition and price sensitive payers. Larger BioPharma companies should be deliberate in establishing different strategies and Operating Models for different business units, ensuring that these match the value proposition that different parts of the organisation deliver.

Case Study

Novo Nordisk:

Doubling down on the next generation of platforms

Novo Nordisk have ramped up M&A activity over the past 5 years, seeking to invest in a new generation of platforms. Their CSO, Marcus Schindler emphasised their shift to a biology driven approach, describing their platforms as a ***'toolbox',*** with Proteins/Peptides, Oligonucleotides/RNAi, Stem Cells and Genome Editing/Gene Therapy all means of targeting Novo's core therapeutic areas.[29] To enable this, they set up ***'Transformational Research Units'*** that operate outside of their core R&D structure to progress the use of platforms like RNAi and Cell Therapy across multiple therapy areas.[30] This structure has been used as means of supporting both organic and inorganic growth opportunities, with their acquisition of siRNA specialist Dicerna used to establish a Transformational Research Unit dedicated to exploring the potential uses of the platform.

- **Operating Model shifts are Time and Execution intensive**

Building the right Operating Model to suit the organisation is not an overnight endeavour. We hear concerns from mid-size BioPharma companies about *'how long it is taking'* to shift the operating model, as it is often assumed that a 6-month reorganisation is the norm. Organisations need to plan Operating Model changes in line with evolving portfolio requirements, potential acquisitions or divestments, and stakeholder needs. Building a roadmap for developing new capabilities alongside an Operating Model structural change can help BioPharma companies go beyond the typical project management approach and timeline for transformation plans, and act as a guardrail for long-term organisational development.

Case Study

Alnylam:

Progressing from a promising platform to an integrated Biotech

Alnylam have evolved over the last 10 years, smartly utilising partnerships to support and fund plans to bring their RNAi Therapeutics to patients. Alnylam's former CEO, John Maraganore, emphasises how partnerships and initial research plans were used to support their ultimate aim of bringing innovation to patients themselves. He cites that the ***'alliances were mostly about funding and external validation,'*** with partnerships and initial development efforts as part of their 'Alnylam 5×15' strategy purposed with developing 5 initial targets to clinical development to clinical stage by 2015. Initial targets were 'liver-expressed, genetically validated disease targets',[31] where probability of proving the platform's potential was stronger. Alnylam's growth highlights the delicate balance early stages companies must take as they develop their Operating Models and identify their source of differentiation. In Alnylam's case taking a platform orientated approach was a necessary precursor to fund their growth and help develop their commercial muscle to progress towards becoming an integrated Biotech.

Realising Operating Model change means be willing to address the key questions

Every BioPharma company is unique. Rather than recommending specific archetypes for company types, we close by suggesting key questions for BioPharma companies to consider, to align and initiate effective change of their Operating Models.

- **What trade-offs are we willing to make?**
  Each archetype comes with an associated set of capabilities, and that can mean trade-offs in investment priorities. Platforms Innovators may dedicate investment to accessing innovative modalities, divesting specific disease-related assets or selling royalties to a Patient Listener archetype; Patient Listeners might need to tailor their portfolio to focus on fewer therapy areas, building commercial and medical capabilities that can scale across these.

- **What is our appetite for risk?**
  Untested modalities and highly contested indications bring significant risks but potentially greater rewards. BioPharma companies must align on the risk tolerance and the cost to their organisations of investing in more speculative assets.

- **What is our timeline for return on investment?**
  The time horizon for RoI can also shape the Operating Model changes planned. BioPharma companies need to be cognizant of how to marry immediate cost control with their growth plans.

The pursuit of new modalities amidst a more challenging pricing landscape means a more dynamic industry with changes in how BioPharma companies align their organic and inorganic strategies to innovate. Their Business and Operating Models must reflect these strategies to capture growth – aligning on the right archetypes is a start.

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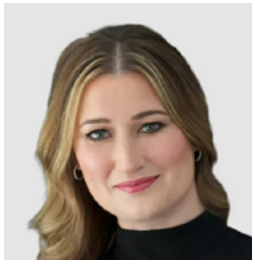

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