Taking the Long View:

Translating Science and Technology Into Commercial Opportunity

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For management at any innovative company, but particularly for an early stage biotech CEO, explaining and extolling his or her company's science or technology platform are important tasks. After all, that's the engine that drives a company's future success. What's more, at the outset of a biotech's existence, it's likely the only concrete attribute to talk about in the first place. But communicating where that engine will take the company and the possible routes management might take to get there is equally essential.

As the first white paper in our series "Growing Up Biotech", we'll discuss the importance of communicating a compelling product story early in a biotech company's existence. It may seem early for a company 10 years or more from gaining approval of its first product to begin positioning that product in the market. Nevertheless, it's important to take a long-term view when implementing this strategy, understanding that the story will need to be revisited often as the company matures. This story should translate science and technology promise into its ultimate commercial opportunities and patient impact for a biotech company's diverse set of audiences, including partners, payers, regulators, patient advocates, and investors.

Beyond the Science

Emerging biotech companies must clearly and repeatedly communicate to a set of diverse audiences the value of the science that underpins their value propositions. But as critical as a company's underlying science and technology are to its story, biotech executives need to think and communicate beyond the scientific promise and technical hurdles they aim to surmount.

Becoming well versed in the company's potential commercial outlook, possible clinical pathways, and regulatory obstacles and opportunities, and being able to articulate these elements is essential. It also positions a company to receive critical feedback from potential partners, future investors, key opinion leaders, and other audiences. Developing a theoretical roadmap from scientific innovation to commercial execution and medical practice helps to underscore the real value of that innovation and advance the perception of a company from "science experiment" to future commercial enterprise. This remains true even as a biotech's growth path evolves in the face of new data, competition, or business development and science-driven opportunities.

Growing Up Biotech

Beginning at inception, emerging biotech companies experience a sequence of hurdles and uncertainties while pursuing the launch of their first product. From the initial conversation with investors and in-licensors to the subsequent steps post-launch, ClearView Healthcare Partners' white paper series "Growing Up Biotech" identifies and addresses strategic clinical and commercial questions companies are likely to encounter while exploring common barriers and critical success factors that are often overlooked.

Knowing Your Audience

Every fledgling biotech should attempt to adequately translate its innovative science into a compelling value story supported by sufficiently rigorous analysis. Those that cannot may be in trouble from the start, particularly if a company's prospective partners or investors understand that opportunity better than management. Later in this paper we'll examine the purpose of developing a thorough communication strategy, the important components of such a strategy that a company must consider, and the pitfalls that can emerge along the way. Subsequent analyses will focus specifically on key biotech audiences, including investors and partners.

Wrapping a commercial product story around even early-stage R&D programs can help various constituencies gain an appropriate understanding of a biotech's goals. That said, the level of detail and focus may vary depending on audience. Management should aim to strike the right balance, and have multiple versions of briefing or background materials to suit each audience. For scenarios where biotechs are seeking capital from investors, communications and materials can include more thorough market sizing exercises.

Back-of-the-envelope approaches may suffice for less-focused audiences. But generally, too few companies sufficiently think these issues through before embarking on the typical biotech presentation circuit.

Solutions Require Problems

Understanding what medical problem you're trying to solve and clearly articulating your company strategy within that context is key to successful communication. Simply having a technology or drug candidate and identifying a disease for which that asset might be useful is not enough. Companies entering highly genericized fields with assets that may be marginally more effective, or safer, than inexpensive incumbent therapies ought to place particular emphasis on why their drug candidate can succeed commercially against or alongside entrenched and accessible competition.

Bermuda-based Axovant Sciences has harnessed positive analyst and investor sentiment by communicating in a sophisticated way about how its lead drug candidate might fit into existing, generic drug regimens that treat Alzheimer's disease symptoms as well as future regimens that could include disease-modifying therapies. Axovant is developing the 5HT6 receptor antagonist intepirdine to improve cognition in patients suffering with Alzheimer's disease, and their communication strategy has remained fundamentally grounded in the epidemiology and high unmet need associated with Alzheimer's dementia, maintaining excitement even amid failed compounds in the same class.

Biotechs that are attempting to address significant unmet medical needs have ostensibly obvious advantages in relating the impact of their science and technology platforms and product candidates to their eventual real-world applications. Take for example the scourge of antibiotic-resistant bacteria. Antimicrobial resistance and other opportunities that have entered mainstream public consciousness may appear straightforward—and straightforwardly marketable. Chapel Hill, NC-based Cempra Pharmaceuticals, one of the disappointingly small handful of companies working to develop new antibiotics, diligently communicated with relevant audiences about the unmet medical need possibly addressed by its lead antibiotic solithromycin, the paucity of competing new antibiotics, and the regulatory incentives it accessed as the candidate advanced through development.

Characterizing the Opportunity

Part of developing and effectively communicating an asset's value story is having a firm grasp on the epidemiology of the disease in the markets the biotech intends to address, particularly for

Axovant Science's communication strategy for intepirdine has integrated many of these early narratives.

THE STRATEGY:

- Remained fundamentally grounded in the epidemiology and high unmet need associated with Alzheimer's dementia
- Candidly addressed the price of existing therapies keeping investors and other constituents grounded about the potential market
- Aggressively communicated regulatory interactions and clinical development plans

unmet medical needs where no therapy exists. When the Brisbane, CA-based biotech Intermune was developing its first-in-class idiopathic pulmonary fibrosis treatment pirfenidone, it helped to shape the public understanding of IPF as a deadly, underserved, and poorly understood disease. Clear communication around a barren therapeutic landscape can boost the prospects of even marginally effective assets entering orphan indications. When the multinational giant Roche acquired Intermune in 2014 for $8.3 billion, the biotech had yet to turn a profit—but clearly had convinced Roche of the value of its key asset.

For drug candidates that may enter markets with existing competition, biotech management teams must possess a strong handle on the market's growth trends and effectively communicate how and where their asset can fit alongside existing drugs. The Alzheimer's-focused Axovant has been refreshingly candid about the price of existing Alzheimer's drugs such as Eisai's Aricept (donepezil) acetylcholinesterase inhibitor, keeping investors and other constituents grounded about the potential market that intepirdine may enter. Other companies with Alzheimer's candidates often cite only a number of sufferers—potentially misleading investors who might be inclined to plug the-sky's-the-limit prices into their models.

Finding Comparables

It is often helpful to cite concrete commercial analogues to a biotech's development-stage candidates to better illustrate a pipeline's real-world opportunity. The antibiotics company Cempra communicated well about the drug candidate's development plan and how it could, as the pharma giant Pfizer demonstrated with the blockbuster azithromycin (Zithromax, Z-pak) in the previous generation of antibiotics, have broad potential utility. By comparing solithromycin to Zithromax, Cempra was able to evoke in investors' minds the success of Pfizer's product, and therefore the market potential for the development-stage antibiotic.

Companies pursuing "me-too" therapies, or products similar to others already on the market that might appear challenging from a regulatory or commercial standpoint, can point to remarks from senior FDA officials lamenting the lack of second-, third-, or even fourth-in-class therapies against particular targets. A case in point is the success of Latuda, Sunovion's late-to-market antipsychotic that boasted nearly $1.4 billion in fiscal 2015 sales for Sunovion parent Dainippon Sumimoto, the Japanese pharma company.

These sorts of analogues can be used to give an early-stage technology the sheen of reality.

Cempra Pharmaceuticals diligently communicated the unmet need possibly addressed by its lead antibiotic, solithromycin.

THE STRATEGY:

- Communicated the paucity of new antibiotics, and the regulatory incentives it accessed during development
- Compared solithromycin to Zithromax, evoking the success of Pfizer's product
- Failed to appropriately communicate expectations for the molecule's regulatory review

Unfortunately, solithromycin was not approved by FDA at the end of 2016 —the regulator is seeking more safety data and raised concerns about a manufacturing plant.

A company like New York-based Intercept Pharmaceuticals, for example, might find a useful comparator for its recently-approved Ocaliva primary biliary cholangitis (PBC) therapy in one of the industry's greatest success stories: the statins. Ocaliva (obeticholic acid) is also being developed for non-alcoholic steatohepatitis (NASH), which could be the drug's biggest market opportunity. NASH, like the hypercholesterolemia so successfully treated by statins, is asymptomatic, affects a similarly sized patient population, and is expected to increase in prevalence.

Identifying Pitfalls

An effective messaging strategy acknowledges and addresses the uncertainty inherent in the drug discovery and development process. Where multiple development paths forward for an asset exist, management should be open about what it does not yet know—about a potential indication, market, or set of priorities. Cambridge, MA-based Sage Therapeutics has embraced this optionality, effectively building a pipeline focused on orphan epilepsy indication therapies but avoiding a narrow focus on orphan indications with its earlier-stage assets. These newer assets are positioned to tackle broader, more common diseases including mood and movement disorders.

Biotech management should also strive to identify potential regulatory, pricing, and reimbursement barriers, and be forthcoming about the future competitive landscape that might await its development candidate should it succeed in running those gauntlets. Alongside a realistic approach to its potential future marketplace, Axovant has been aggressive in communicating about regulatory interactions and clinical development plans for intepirdine. The strategy has paid off in spite of the failures of other 5HT6 drug candidates by creating excitement around their molecule as a possible best-in-class treatment. Intercept's engagement with regulatory authorities around disease settings for Ocaliva, including in NASH and PBC, helped to illuminate challenges and opportunities along each development pathway.

The antibiotic developer Cempra may have succeeded in mapping out the unmet need for its drug candidates, hammered the benefits of its regulatory incentives, and attempted to illustrate its market potential for solithromycin with an historic comparable product in Z-pak. But in failing to appropriately manage expectations for the molecule's regulatory review, adequately articulate the possible reimbursement distinctions between in- and out-patient settings for its drug candidate, and the eventual market limitations that may stem from antibiotic stewardship, the company helped to create a disconnect between management and

> "An effective messaging strategy acknowledges and addresses the uncertainty inherent in the drug discovery and development process."

investor expectations. Solithromycin was not approved by FDA at the end of 2016 as Cempra had hoped—the regulator is seeking more safety data and raised concerns about a solithromycin manufacturing plant.

Pipeline in a Product

Finally, it's never too early for biotech management teams to think about the life-cycle management opportunities that may await a successful development program. Intercept's Ocaliva, with its approval in PBC and continued development in NASH and primary sclerosing

cholangitis (PSC), illustrates well the pipeline in a product phenomenon that has created many industry blockbuster drugs.

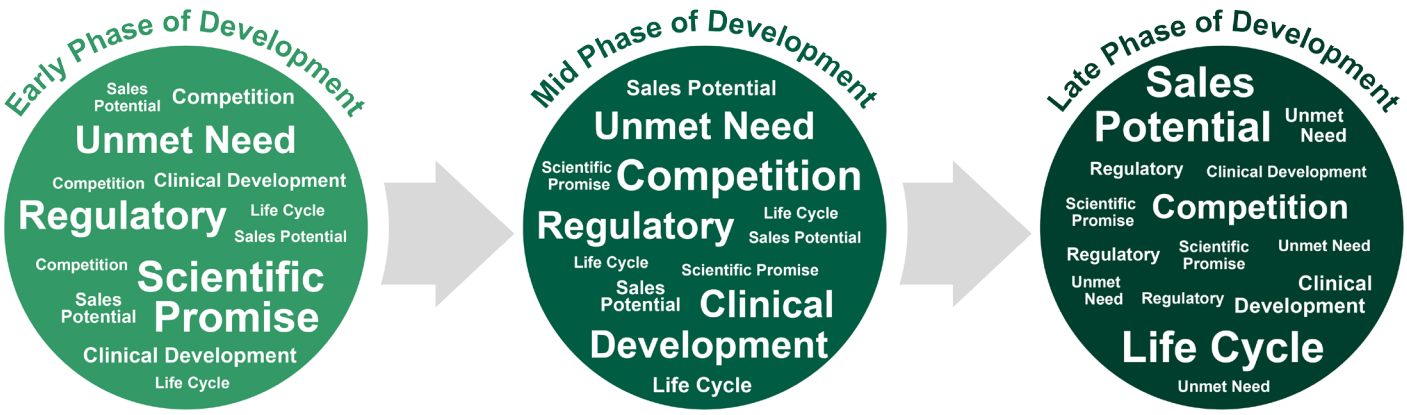
Building out a pipeline from a single therapeutic candidate isn't realistic for every biotech company. Capital constraints may certainly play a factor. But effectively fleshing out and communicating a broader development plan that future partners might pursue, or future investors might enable, is an important part of building a drug candidate's value proposition. This is particularly important when developing assets in clinical settings where combination therapy is de rigueur, such as immuno-oncology, and where a single small biotech is unlikely to possess all the components itself. San Francisco-based Five Prime Therapeutics' cabiralizumab colony stimulating factor 1 receptor inhibitor antibody held promise in multiple oncology settings, in combination with a variety of checkpoint inhibitors – including Opdivo and Yervoy, from the big pharma Bristol-Myers Squibb Co. In 2014, Five Prime teamed up with BMS in the clinic, initially to test cabiralizumab in combination with Opdivo in six tumor types, in an R&D deal where Five Prime retained rights to its candidate. A year and a half later, convinced of the asset's broad potential, BMS decided to license rights to the Five Prime antibody in a deal worth $350 million up-front.

The Long View

Biotechs that are able to envision a commercial future for their early-stage assets or technology platforms and communicate that future to a diverse set of audiences are well positioned for success. Those that fail to look – and communicate – beyond the scientific excellence and promise they already possess may wind up failing to understand their own potential.

Messaging and materials about a company's path forward, the commercial opportunities that await its drug candidates, and the clinical, regulatory, and access challenges that await it along the way can and should be tailored to a diverse set of audiences. These will no doubt be modified as a biotech matures, as it fails, or even as it succeeds beyond expectations. What must be constant is management's focus on its ultimate commercial and medical goals, and the ability to explain to partners, investors, payers and others, how it can execute in order to reach them.

As you progress through the development phases, you'll want to bring different components into focus



About ClearView Healthcare Partners

Founded in 2007, ClearView Healthcare Partners is a global strategy consulting firm serving the life science sector. The firm combines international industry knowledge and deep scientific expertise across a range of therapeutic areas with an extensive network of external stakeholders to deliver practical and actionable recommendations to our clients' most complex challenges. The firm's projects include cross-functional support at the corporate, franchise, and product levels for pharmaceutical, biotech, medical device, and diagnostics companies worldwide.

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