To Partner or Not to Partner:

Determining Your Commercialization Plan

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Deciding whether to partner an important late-stage asset or commercialize it independently is a biotech dilemma as old as the industry itself.

An emerging company aims to maintain as large a share of equity in its lead asset as it can. At the same time, a biotech needs to assess whether tapping the resources of a larger and/or more experienced organization would maximize the product's commercial success. A partner with deep pockets and broad commercial expertise may translate into an increase in market share and therefore increase overall value, which could more than make up for loss of full ownership.

Making the best decision on whether to partner and with whom to partner will depend on many factors including the size and length of clinical trials, access to prescribers through a sales force and medical science liaisons, and ease of market development and access. In this white paper, we highlight the key elements an emerging biotech should consider when evaluating whether to launch a critical asset on its own or seek a partner for commercialization.

This white paper is the second in our "Growing Up Biotech" series, and follows "Taking the Long View: Translating Science and Technology into Commercial Opportunity". In this paper, we identify the key factors around a pivotal question posed when launching your product: to partner or not to partner?

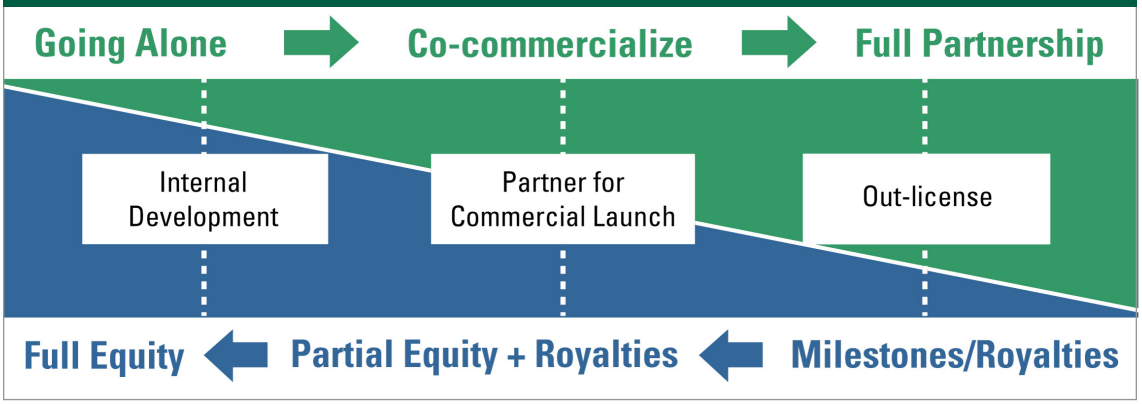
Growing Up Biotech

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.

Where to Begin

Your company has successfully managed the crucial early-stage hurdles of financing, clinical proof-of-concept, and early clinical development of the lead product candidate around which you have built your story. Now with an eye towards commercialization, the question is: how far can or should you run with it on your own?

Partnering Options and their Impact on Your Equity



Source: ClearView Healthcare Partners

Decision Factors

The first step in deciding whether and with whom to partner is to evaluate the extent to which existing clinical development, medical affairs, and sales capabilities are sufficient to support development and commercialization of the asset. In the context of late-stage development, these capabilities are critical to ensure appropriate pivotal trial design and execution. These three pivotal capabilities help balance cost and length of clinical development as well as assist with adequate and timely patient recruitment.

The capabilities and funding for executing the minimum clinical trial needed for regulatory approval may exist internally. Rare disease biotechs are often founded by clinical experts in the field, which provide the scientific knowledge base internally. Increasingly, hospitals and other academic institutions are becoming initial investors or partners of companies developing less traditional modalities that the investment community and corporate partners view as too risky at the outset. For example, Philadelphia-based Spark Therapeutics' technology was born out of the Children's Hospital of Philadelphia's labs, and Seattle-based Juno Therapeutics was a collaboration between three different institutions to develop immunotherapy drugs (e.g., CAR-T cells). In these cases, the founders may be equipped to carry the development ball farther down the road towards approval, particularly as the nature of rare diseases often allows them to run trials that are highly concentrated and focused.

There are other key areas of talent needed for commercialization outside of the initial clinical expertise needed for development. An immediate need in late-stage development is clinical trial recruitment expertise. Familiarity of known and potential drivers of value for clinicians and payers is also important pre-launch as development can be shaped to fill their needs. Relationships with key opinion leaders (KOLs) and key prescribing groups are essential to market penetration and uptake, which takes an experienced medical science liaison to develop and maintain. Additionally, companies need to utilize a sales force tailored to the depth and breadth of the disease's calls points. From a regulatory perspective, talent should be employed to ensure a smooth dialog with regulatory agencies to avoid a delayed launch. Finally, the ability to finance both pivotal and supporting clinical trials and the talent needed to cultivate a strong commercialization strategy is often the ultimate factor that determines a biotech's decision. Alternatively, a company may be able to gain the capabilities easily through contracting, vendor relationships and shrewd hiring, which would help it retain equity in the product.

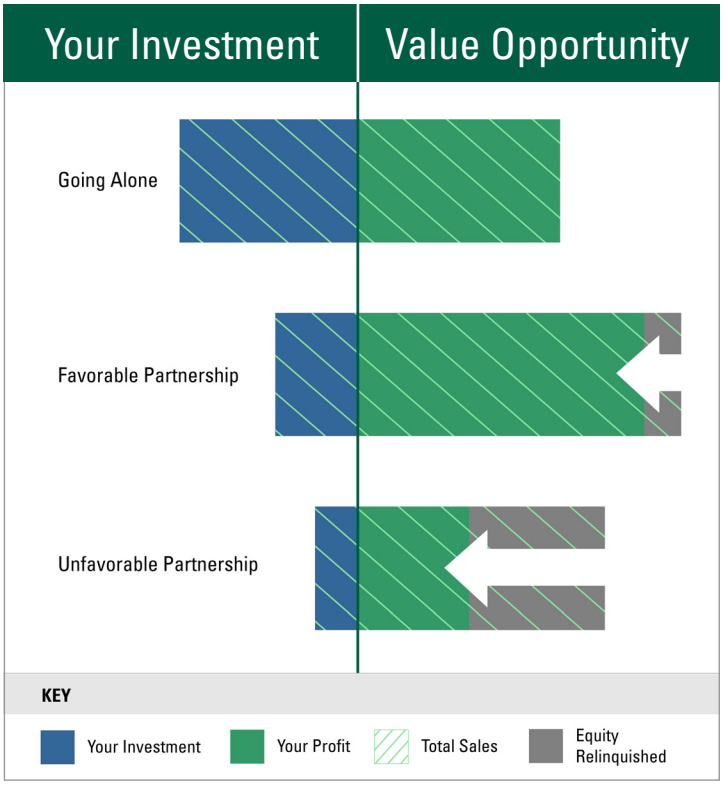
Assessing Internal Capabilities

In parallel with ensuring the sufficiency of late-stage clinical development capabilities, a company should conduct an assessment of what it takes to access the market at and after product launch. Many emerging biotechs choose to address areas of significant unmet medical need. In many of those cases (often involving rare genetic or other orphan diseases), substantial market development may be required to establish a treatment paradigm. Physicians may need to be made aware of the disease and the method of treatment. In rare diseases, a parent will often bring their child to multiple specialists before identifying the disease. The ability to identify, or develop a new, diagnostic path is crucial in areas without current treatments or standards of care. For genetic diseases treated with enzyme replacement therapies, for example, no ready biomarkers exist and extensive enzyme assay development is needed to assure accurate diagnosis.

In such situations, it is critical to determine whether the company is positioned to handle

the investment required for peak utilization by optimizing patient identification (accelerating and increasing diagnosis), increasing patient urgency to be treated, and ensuring the patient experience is consistently positive (enabling adherence and persistence). This set of tasks places a heavy burden on an internal medical affairs organization, to better understand the natural history of the disease, the novelty of the treatment strategy, follow-up with registries and with post-marketing studies to measure real-world outcomes. The challenge is even greater when seeking global coverage: some parts of the world will not be able to access a therapy in the same way that others can, and even in the most sophisticated health care systems patients are still missed.

In light of these barriers, a small, highly specialized sales force may be all that is needed to be commercially successful. That will depend on whether the sales' call points are concentrated (e.g., Centers of Excellence), either because only one specialty is involved in treatment or only a small number of identifiable physicians treat the condition. To some extent, the prevalence of a disease is a factor here, but not always. In cancer, for example, a launch focused on leading tertiary care centers may be appropriate, with the expectation that awareness of the drug will trickle down from these academic prescribers to community hospitals relatively quickly.



Source: ClearView Healthcare Partners

Maximizing the Commercial Opportunity

Once an internal capabilities assessment is done, a management team can balance the benefits of maintaining full equity in the product against the costs of building or buying the capabilities needed to maximize the value of a new therapy. Knowing what a company can afford to do on its own will influence whether it should seek out a partner with deeper pockets and experience in the disease space.

Several factors will determine the amount of spending required to take a late-stage product candidate to the market. These include the number and size of the patient populations for potential indications, the extent to which those markets are well defined and accessible, and the practicality of splitting indications with a partner. Paratek Pharmaceuticals, for example, opted to out-license its narrow-spectrum antibiotics for treating acne to Warner Chilcott (now part of Allergan) in 2007, given the broad call points (PCPs and dermatologists) and the affected population.

In many situations, collaboration will add value when the partner is the leader in the disease space. A partner may have strong KOL relationships and/or brand awareness in areas where significant market development and awareness is required for which the owner of the asset does not have the resources.

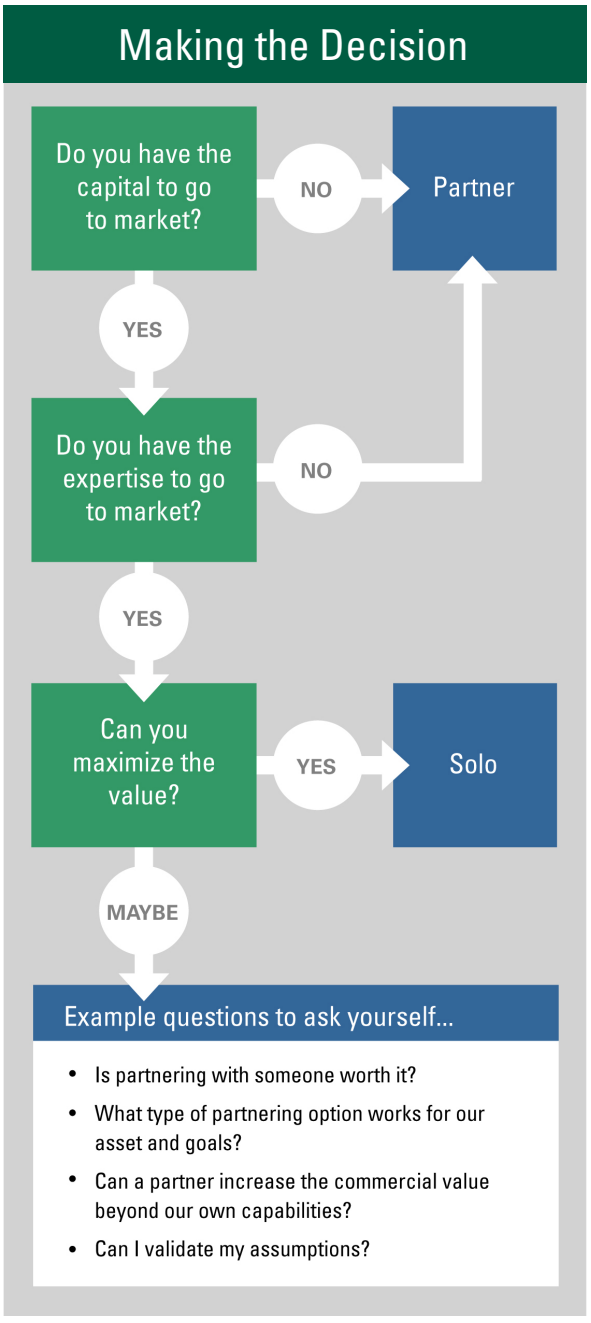
If, on the other hand, a company has the financial resources to afford to take more time in clinical trials in order to show a bigger benefit, it may refrain from partnering in order to further build up asset value – particularly in rare diseases where the treatment paradigm is not well defined. Similarly, having the resources to commercialize a small indication for a drug (or advancing the data in a small indication for a drug with potential wider use) could help pave the way for a larger deal down the road.

Having a treatment for a rare disease does not necessarily mean that patients will be concentrated around a call point, or that it will be easy to define the target audience for any requisite market development. In HoFH (homozygous familial cholesterolemia) and other rare cardiovascular indications, for example, a concentrated set of academic lipidologists manage the majority of treatment decisions, but PCPs and cardiologists are important call points to ensure rapid and appropriate referral pathways. Similarly in Rett syndrome, a very rare disease, patients may see a neurologist, a cardiologist, a pediatrician and a geneticist, making the commercialization process more complex because of the need to hit multiple call points to access all the patients. On the other hand, a developer of a drug to treat Rett could decide to focus on pediatric epileptologists, retaining commercial rights for that market but not for others.

Types of Partnerships & Finding a Good Fit

If an emerging company decides its interests are best served by partnering, the terms of that partnership will in part turn on who is in the best position to lead the commercialization process, including the management of late-stage trials. Partnering options range in scope from contracting for a sales force to co-commercializing in designated geographies to out-licensing and retaining only royalty revenue.

The extent to which a company has or wants to develop sales and marketing capabilities, often in one or more defined geographies, may be a major factor in choosing a partner and in the amount of equity in the product a company is willing to forego to maximize commercial opportunity.



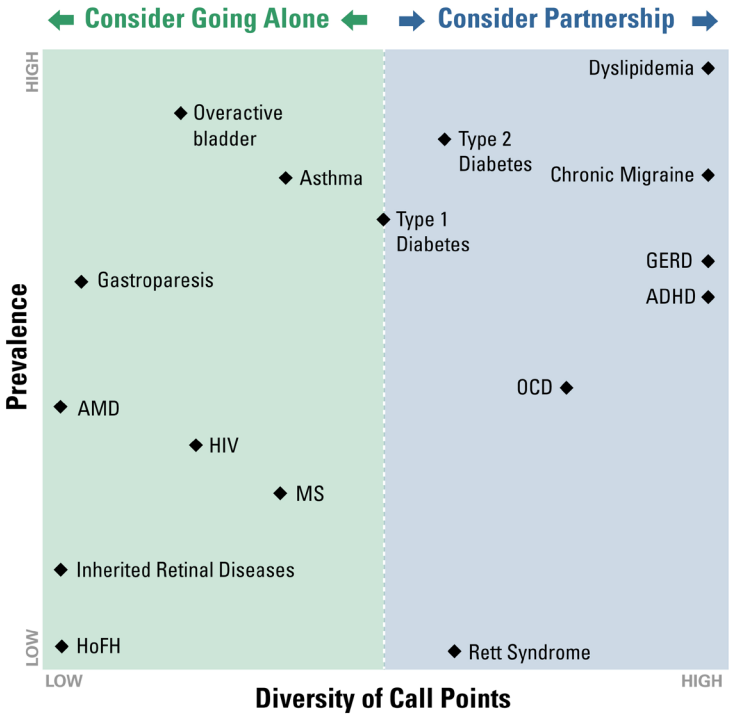
Source: ClearView Healthcare Partners

Building rather than partnering for a sales force may make more sense if, down the road, a company wants to leverage the same call point for future products. Managing the first indication may be expensive and other companies may be better suited to make the most of the lead product, but the investment might be worthwhile due to the longer term benefit of having the sales force available for the rest of your portfolio.

An agreement to co-promote or to license only certain territories can achieve this objective, and also bring in significant cash up front. The upfront payments and milestones from a partnering agreement can help fund additional corporate activities, either around different indications for the same drug or to support development of other drugs. Assessing the need for such an immediate return is a key consideration for many emerging companies: money now is worth more than money later.

Partnership for Commercialization

While low prevalence indications and rare diseases often have centralized call-points, there are exceptions. Rett syndrome affects the respiratory, neurologic and cardiovascular system creating a standard of care across many types of physicians.



Source: ClearView Healthcare Partners

Exelixis's signature 2016 deal around its lead cancer drug Cabometyx checked off many of these boxes. Two months before receiving FDA approval for the treatment of advanced kidney cancer, the biotech company inked a deal with Ipsen for rights to Cabometyx outside of the United States, in Europe and Japan. It received $200 million upfront plus development milestones including additional indications, and associated royalties. The deal allowed Exelixis to sell off Japanese and Canadian rights separately. Moreover, it helped fund its United States launch of the drug and reinvigorate internal discovery research. The deal also provided the opportunity to generate more funding for Cabometyx as more data came out. Ipsen is also now supporting Cabometyx's development as a combination therapy with immuno-oncology drugs through an opt-in it exercised in 2017, and still open are possibilities for funding of work in lung and other cancers.

Lexicon Pharmaceuticals is another example where partnering helped achieve several critical goals. The company, focused primarily on the development of a compound aimed at treating type 1 and type 2 diabetes, had downsized early in 2014 and did not have the resources to handle a large diabetes program. It stopped work on the type 2 program to focus on type 1, a more manageable indication for a small company. The downsizing also enabled it to move a second drug, Xermelo, forward in carcinoid syndrome, which Lexicon then partnered with Ipsen later in the year, ceding ex-US rights. The money from that deal also supported the diabetes program, which a year later Lexicon partnered with Sanofi, retaining an option to co-promote with Sanofi in the US.

Risks of Partnering

An attractive product candidate will often draw inbound interest from a variety of suitors, and some will be a better fit than others.

The interests of a partner will also vary. For example, while speed to market may be critical for an emerging company, a partner with its own internal portfolio may have a different appetite for risk and only be comfortable with a "belt and suspenders" approach that is lower risk and longer, to increase the likelihood of clinical and regulatory success. The composition of a partner's portfolio is also a consideration as it may contain compounds that possess a similar mechanism of action or target the same set of patients. Data emerging on those during the development phase of a partnership could lead to its de-prioritization or, if the product is competitive and not complementary, even cannibalization.

Making the Decision

The decision to partner and with whom to partner is not a cookie-cutter process, and each deal lands on a wide spectrum of options. Companies want to maintain control and maximize the value of their asset, however a partnership will create trade-offs. We offer some guiding principles, but a company will have its own unique set of resources, requirements and options. When first making these decisions, it is crucial that emerging biotech's assess their internal technical and financial capabilities for commercialization. Calculating the variable levels of equity versus commercial success allows companies to think about and prepare for different partnering options, which include an assessment of risk in each scenario. Ultimately, biotechs should play out each scenario to determine the right balance regarding a drug's potential value and the amount of equity and control.

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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