From the Board Room

Early commercial assessments: An innovative tactic for small biotechs

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ABSTRACT

As a small biotech company embarks on a drug development program, there is a tendency for management to focus on a well-defined set of issues. Is the science behind the drug valid? Does it solve an interesting problem or unmet need? What are the prospects that the medical community and patients will embrace it as a valuable new solution? And what is the range of indications the drug is conceived as addressing? These are all valid questions, but a small biotech can do even more to prepare itself for the drug development process, which is a journey that can take many years and cost a significant amount of money.

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One of the most important extra steps the company can take is to assess the existing commercial landscape relative to the unmet medical need, in order to analyze the eventual demand for their new drug. This analysis is based on a projected target profile and projected pipeline competition, which also requires successful clinical trials and FDA approval. The earlier in the drug development process these assessments occur, the better. Although some CEOs might question the need for an early commercial assessment—in light of the extensive time and planning that is involved—there is ample evidence that, done properly, it can be a uniquely powerful tool to demonstrate and maximize a drug's value. It can give a small biotech a major advantage as it embarks on the drug development process, especially informing clinical trial design, for example, primary and key secondary endpoints. Most importantly, the biotech can speak confidently with capital providers and potential pharma partners about what is important to these stakeholders: namely, how many patients are likely to use the drug; why would they need and accept the drug; what other drugs offer the same solution; and who will pay for it and why.

Our company, Cynapsus Therapeutics, conducted an early commercial assessment process based on our drug candidate APL-130277, for which we are now planning Phase 3 trials. The drug is a sublingual formulation of apomorphine, an on-demand medication for Parkinson's disease patients suffering from hypomobility "off" episodes. Currently, apomorphine is only available as an injectable product that is usually administered by caregivers. The existing product's delivery mode and poor tolerability profile have limited the use of this potent and effective therapy. APL-130277, in contrast, enables absorption directly into the bloodstream through the oral mucosa and can be easily self-administered in many cases.

Our first step was to establish the overall goals of the assessment. Foremost among these was to broadly analyze the commercial potential of APL-130277 for Parkinson's patients in the U.S. and Europe who experience "off" episodes. However, we established a series of related secondary goals as well: to understand the

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prevalence of "off" episodes and our drug's potential role in the treatment paradigm; to assess the competitive environment; and to clarify market access issues and the pricing and reimbursement landscape. In addition, we wanted to develop, modify and validate target product profiles for APL-130277 and determine how the potential market size would likely be influenced by its novel route of administration and potential clinical, safety and tolerability attributes.

To achieve these goals, we initiated a campaign of primary research that comprised the use of independent consultants and interviews with 775 neurologists internationally, 37 Parkinson's patients and 53 major payors across the U.S. Our primary research also included physician and patient interviews to obtain quantitative feedback. In addition to these primary sources, we consulted a wide variety of secondary sources of data, ranging from the National Parkinson Foundation to the U.S. Census Bureau, as well as our own prior primary research (i.e., surveys of neurologists and payors) to inform our analysis. A special focus of the assessment was the revenue potential of the drug in the U.S., which we analyzed across several revenue scenarios involving varying adoption levels and frequency of use.

The results we obtained from this assessment were both comprehensive and informative. For example, they provided us with:

- **An improved understanding of the potential customer base for the drug.** "Off" episodes affect around 50 percent of the approximately one million Parkinson's disease patients in the U.S.; the incidence of the episodes tends to be relatively high in moderate to severe Parkinson's patients who have a history of dopaminergic drug use.
- **An insight into the drawbacks of existing treatments.** Apokyn, currently the only medication approved to treat "off" episodes, has had limited usage in the U.S. due to critical barriers such as unfavorable route of administration and lack of convenience associated with an injection.
- **A clarification of the unique benefits of our drug formulation.** APL-130277 is a rapidly dissolving thin-film vehicle incorporating stabilizing ingredients with apomorphine in solid form, plus pH buffers to enhance stability, lower irritation and maintain optimal absorption. Rapid uptake results in efficacious concentrations quickly.
- **A better picture of the competitive landscape for our drug.** We analyzed five direct competitors to APL-130277 (compounds that either act as rescue medications or have the potential to lower the "off" time and cycle) as well as 11 indirect competitors (that reduce the "off" time and thus lower the frequency/dose of the rescue medication).
- **A good indication of necessary next steps to educate.** Prescribers, nurses, patients and caregivers all need to be informed of the potential of apomorphine to address "off" episodes, as well as the specific advantages of oral delivery. A multi-stakeholder communication program is therefore a necessary initiative for us.
- **Estimates of the potential market opportunity for our drug.** We have generated annual revenue forecasts and annual unit consumption forecasts for APL-130277 through the year 2030, assuming a "best case" (in which our drug is launched with no major competitors other than Apokyn) and a "probable case" (in which our drug is launched with other direct competitors). We also had an independent consulting group produce a similar study based on their primary and secondary research.

A prime factor shaping the course of the commercial assessment was the unmet need for a new treatment, as perceived by three distinct populations: patients, neurologists and payors. The burden of "off" episodes and the lack of practical treatment options result in a large unmet need for a rescue therapy that is effective and easy to administer for patients and their physicians. Survey responses from each of these three sectors suggest that APL-130277 has the potential to grow the limited apomorphine market in the U.S. driven primarily by increased physician adoption and greater patient acceptance.

Survey results suggest that patients would benefit from a quick-acting, easy-to-use drug such as APL-130277 to treat "off" episodes that provides relief from the quality-of-life burden without imposing a high treatment burden; currently, when presented with the opportunity to use Apokyn, most patients choose not to initiate treatment, primarily due to the injection and possible skin irritation and inflammation. And among those who do begin treatment, around 50 to 75 percent tend to drop out of therapy. Patients are enthusiastic about APL-130277 and suggest they are likely to discuss it with their neurologists. One patient commented, "I would not want to use the injectable version…I don't like injections.

The strip would definitely be very easy for me to use, and I wouldn't mind using it, and it wouldn't be as conspicuous as the needle."

Meanwhile, neurologists indicate a positive attitude toward APL-130277 and see it as a promising potential therapy, based on its quick-onset action of 10 to 15 minutes and its easy-to-use sublingual formulation. Neurologists suggest a greater likelihood to prescribe APL-130277 over the injection to their Parkinson's patients and expect a much greater patient acceptance rate for it. For many neurologists, the complex initial titration and patients' reluctance to use shots cause them to avoid adopting the injection into their practice. One neurologist commented, "I haven't used the injection because it's complicated…I think [APL-1302767] is definitely worlds better than the injectable type. It will be easier to administer… Nobody wants to inject themselves. But anyone can take six little sublingual doses." Another neurologist said, "there's a much, much lower threshold for recommending APL-130277 and for patients' acceptance."

Payor feedback suggests they would view APL-130277 similarly to other branded Parkinson's disease therapies (e.g. Apokyn) and would place it in a non-preferred branded tier without restrictions in commercial and Medicare plans.

Of the approximately 400,000 U.S. Parkinson's patients who experience "off" episodes, less than one percent is currently treated with injected apomorphine, whereas a survey of 500 neurologists indicates that up to 49 percent of all patients would be candidates for treatment with sublingual apomorphine. Furthermore, each of these patients is expected to use a more convenient sublingual product much more frequently. Most payors already list apomorphine as medically necessary, and inclusion of APL-130277 in formularies will only require the consent of providers' pharmacy and therapeutics committees, which typically meet at least quarterly. The technical challenges overcome to create this formulation provide extended patent protection, limiting the expected competition to only a few players pursuing alternative routes of administration of Levodopa Carbidopa, which is not approved to treat "off" episodes.

The early and continuous commercial assessment process conducted by my company has given us a substantially clearer picture of the challenges we face, as well as a powerful marketing tool to share with potential investors and partners. I have little doubt that any small biotech—conducting an early and continuous assessment process on a similar scale for its own drugs in development—will find the insights it can provide to be equally valuable.