blue matter
RARE DISEASES

The Breakfast Club "Bottom Line"

Summary of Key Points from the First Blue Matter Breakfast Club™ Meeting

Zug, Skylounge, 20th March 2019

Presentation Summary

The Breakfast Club meeting of 20th March 2019 included an initial address by Dr. Flemming Ornskov, former CEO of Shire Pharmaceuticals. Following Dr. Ornskov's address, the broader group engaged in an interactive roundtable discussion.

The summary below is intended to capture the "bottom line" of the discussion in an extremely concise, well-organized manner. Key themes from the session are captured here as notes for attendees and for other interested readers. None of the key points or themes related below should be construed as being attributed to any one individual. Rather, these notes are intended to provide a general overview.

Key Theme 1 – 'Riding the Big Wave': Rare diseases present an enormous opportunity.

1. A significant unmet medical need persists in rare diseases (RDs). Less than 5% have an approved treatment today. Unfortunately, most are of genetic origin, manifest early, and disproportionately affect children. While individual RDs are rare, collectively they affect a very significant number of people. This unmet need is driving added focus in the space.

2. "Riding the Big Wave" was a central theme of the discussion. The rare disease space presents a very large business opportunity, and it was compared to a building wave.

3. A number of factors have helped to create this wave, including
   a. Progress in policy work (including the Orphan Drug Act of 1983, a highly successful policy that created significant positive impacts for patients and created jobs)
   b. The recent development of highly specialized treatments
   c. Increased understanding of numerous rare diseases
   d. Progress in diagnostic techniques and technologies

4. Historically, a few pioneers have operated in the RD space, including Shire, Genzyme, Biomarin, Alexion, and others.

What is the Blue Matter Breakfast Club?

As a strategic consulting firm serving the life science industry, Blue Matter works to remain on the leading edge of commercial strategy in biopharmaceuticals.

The Blue Matter Breakfast Club is an ongoing series of quarterly 2-hour breakfast forums, hosted by Blue Matter's rare disease team. These forums bring together leaders from companies that develop and commercialize rare disease therapies to discuss critical business issues. They are by invitation, and they offer a private, engaging environment for networking and discussion.

To inquire about speaking at or attending a Breakfast Club event, please contact:

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5. As the business opportunity has grown, large biopharmaceutical companies have been entering the market over the past 5 years, such as Novartis, Pfizer, Roche, Sanofi, and others.

6. Investments in the rare disease space have increased rapidly in the last few years, driven by biopharmaceutical companies, venture capitalists, and others. The recent compound annual growth rate (CAGR) in investment has been 11%+. That is forecast to continue for the next two years (and likely far beyond).

7. Rare disease is not a small business anymore, as the current market size is around $140 billion per year.

8. Recent acquisitions and revenues show that rare disease is a large field. This current high level of interest will bring even more money to research and development and will enable the development of treatments for various diseases that are currently under-served.

9. It is likely that many more traditionally big market leaders will move towards a rare disease model, as driven by personalized healthcare (PHC) companies that focus on increasingly smaller patient segments, even within big therapeutic areas (e.g., cardiovascular).

Blue Matter Perspective / Industry Implications:

1. The $140 billion RD market will grow to about $216 billion in 2022. However, the potential is far greater. An estimated 40 million patients in the US and EU are affected by rare diseases. Assuming an average "one time" treatment cost of $100,000 (which is conservative, given the high-cost nature of many RD therapies and costly future treatments with curative potential such as gene therapy), the market's theoretical potential is $4 trillion.

2. Competitive pressure will increase in the more "crowded" RD disease areas. Examples include degenerative neuromuscular diseases such as spinal muscular atrophy and Duchenne muscular dystrophy. It will be important for companies to find appropriate niches, understand their competitive situations, and continue to innovate and differentiate, particularly in disease areas without any treatment options today.

3. As the use of precision medicine increases, common diseases will "morph" into more rare diseases, as they are "carved up" into increasingly well-defined patient segments. Companies will need to develop an understanding of RD business & customer engagement models, and then adopt those models for more common diseases. Those models are highly patient-centric, are "high-touch" with key customer groups, and require a customized organizational structure to implement effectively. Those that do this successfully will gain an important competitive advantage.

Key Theme 2 – Technology will have a dramatic impact on Rare Diseases. PHC, Telemedicine, "Big Data", and Artificial Intelligence (AI) represent significant future opportunities.

1. Innovation in diagnostics is accelerating dramatically.
   a. Genetic diagnostics, in particular, are exploding.
   b. Diagnostics in RD will further accelerate success in the field; the combination of PHC and diagnostics innovation will be the future.
   c. Given the momentum toward PHC and companion diagnostics, it's likely payers will restrict reimbursement unless companion diagnostics have been able to identify the right patients for the right treatments. It is already happening in some cases.

2. Telemedicine will improve care, empower patients, and boost research.
   a. What is currently happening with telemedicine in RD will be predictive of what will happen in biopharma. Telemedicine helps to find patients, improve physicians' disease knowledge, have more predictive diagnostics, and provide continuous monitoring of patients.
   b. Technology will be a key driver of future patient empowerment. Patients will participate a lot more in selecting the right treatments and in managing their diseases.
   c. Patients will be able to request different therapies and treatment approaches. For example, a patient will not hesitate to seek a prescription from a health care expert in the US using data on the cloud, rather that visiting the local physician next door.
   d. In 5 years, all RD patients will be going to physicians or healthcare providers with a device carrying their genetic information that will be critical to establishing a clear diagnosis, determining the right treatment option, and predicting outcomes. This technology will also enable participation in large research efforts.

3. "Big Data" and AI will have a significant impact on the RD field, but data privacy will be a challenge.
   a. Big genetic data plus AI might transform the field by revolutionizing diagnosis (e.g. IBM Watson) and predicting the best possible therapeutic options (e.g. Evidation Health).
   b. Large databases and artificial intelligence will have a significant impact on the entire treatment flow

for RDs. They will help support physicians in their diagnoses and prescriptions. They will also make clearer the links between treatment choices and clinical outcomes. This will improve our ability to predict patient outcomes.

c. How to share patient data while protecting data privacy is a societal problem that we will need to solve. One way to solve it is to provide access to anonymized databases that RD companies can buy into.

d. Technologies such as blockchain will be critical to secure and trace genetic information back to the patient as owner, as well as protect data privacy. This will also enable innovators, and potentially also patients, to monetize this critical patient information.

Blue Matter Perspective / Industry Implications:

1. Technology will change the way RDs are diagnosed, treated, and monitored. Biopharmaceutical companies should make an effort to understand the key trends & innovations, seeking partnerships where needed to create value for patients and realize completely new opportunities.

2. Innovation & disruption will likely come from unexpected sources. Examples might include firms like Google, Amazon, Apple, and other tech innovators entering healthcare.

3. Mapping the field and understanding the innovations—and the innovators—will be critical for healthcare players.

Key Theme 3 – Payer models are pressured to evolve quickly.

1. Innovative treatments and tools, such as gene therapy, CRISPR, etc. will directly challenge the traditional pharma model, and new pricing and reimbursement approaches are needed. Driven by the US, the global pricing and reimbursement model is under enormous pressure and will have to change.

2. To address reimbursement challenges, RD companies will not have to think about money issues but rather, financial issues.

3. With gene therapies coming soon, such high-cost treatments will lead payers to ensure that patients have the strongest chances of getting the best possible outcomes.

4. Policy makers and payers will have to consider alternative solutions such as subscription models, amortization, outcomes-based pricing and payment models, and so on. Companies will also have to provide some of their product for free. Industry must be rational in its pricing model.

5. Collaboration among a range of stakeholders is key to solving this issue. Consider the example of a family whose child has an RD for which a gene therapy exists. Despite the high cost of treatment, the family will find a way to do it. They will collaborate with various stakeholders to find a solution. They may reach out to a foundation, etc. RD companies should consider a parallel course: Everybody (biopharma companies, patients, payers, KOLs, diagnostics firms, etc.) need to sit at the table to collaborate and find a solution.

6. Building clusters or an "ecosystem" is the key: Investors for money, companies to create treatments, diagnostics firms to manage the data, and smart people, e.g. from academic institutions, to integrate this to the ecosystem.

Blue Matter Perspective / Industry Implications:

1. Gene and cell therapy, as well as gene editing, will transform the way RDs are treated. A huge wave of innovative new treatments is coming to the market soon.

2. Current payer models are outdated and characterized by a 19th century mindset. They are not currently aligned with these high-cost, often "once and done" therapies. Costs for effective and potentially curative gene therapies might well exceed costs of $1 million US and require completely new payer models.

3. Biopharmaceutical companies must partner with key stakeholders, such as payers & policy makers, to drive novel payer / financing models.

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RARE DISEASES

Passion. Mindset. Experience.

Together, Improving the Lives of Rare Disease Patients.

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