blue matter
RARE DISEASES

The Breakfast Club "Bottom Line"

Summary of Key Points from the 2nd Blue Matter Breakfast Club™ Meeting

Zug, Skylounge, 17th June 2019

Guest speaker: Nick Leschly, CEO of bluebird bio

The Breakfast Club meeting of 17th June 2019 included an initial address by Nick Leschly, CEO of bluebird bio. Following Nick'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 a concise, well-organized manner. Key themes from the session are captured here as notes for attendees and other interested readers. None of the key points or themes below should be construed as being attributed to any one individual. Rather, these notes are intended to provide a general overview.

Recoding for Life - The bluebird bio Story

Key Themes:

1. After a decades-long journey (including an interesting path for bluebird bio), gene therapy is finally delivering the medical breakthroughs that it promised.

2. A relentless focus on the patient is absolutely foundational.

3. The next frontier will be overcoming challenges to realize gene therapy's enormous potential, also commercially.

4. Visionary leadership, risk-taking, and changing current models and mindsets will be key to realizing the promise of gene therapy.

Key Theme 1: After a decade-long journey (including an interesting path for bluebird bio), gene therapy is finally delivering the medical breakthroughs that it promised.

1. Going back to 2003, times were dark for gene therapy as a field. The US FDA and other regulatory bodies around the world had just shut down numerous gene therapy trials due to significant safety concerns. There was only a limited understanding of gene therapy's mechanisms, efficacy, safety, and so on.

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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2. Things began to turn around in 2006 when an Italian research group from the San Raffaele Telethon Institute for Gene Therapy enabled a stable gene transfer, overcoming a major hurdle to successful gene therapy. Nature Medicine 12, 585–591 (2006)

3. Then, a movement was created when GSK and Novartis entered the field of gene therapy in 2009/10. At the same time, research data showing efficacy in two children with beta thalassemia and one child with adrenoleukodystrophy (ALD) were published in Nature and Science respectively. For the first time in history, patients with such rare conditions were alive thanks to gene therapy.

4. At that point, the world "opened up," people were ready, and the science clicked in. The time was right for Third Rock Ventures (where Nick Leschly was working at the time) to enter the field by investing $~30 million in Genetix Pharmaceuticals (which would later become bluebird bio).

5. In September of 2010, Nick Leschly (CEO) and Mitch Finer (CSO) wanted to rebuild the image of the company. With a passion for skiing and beautiful "bluebird" days, they decided to rename the company "bluebird bio". The idea behind the name was to give patients the opportunity to experience their "bluebird" day and to create a positive company culture.

6. After nearly 10 years, this culture is still present. 900 people were at the recent bluebird offsite meeting, and the atmosphere felt like a revival. The team's success is, in large part, driven by their focus on the purpose behind their work: To save lives.

7. During bluebird bio's journey, other companies demonstrated the benefits of gene therapy, as well. Novartis (with CAR-T therapy and Emily Whitehead, the first pediatric patient to receive CAR-T therapy…and she's still in remission), GSK (Strimvelis), and others all contributed to the advancement of gene therapy.

8. Today, we are still on the "steep side of the curve" from a scientific standpoint. There are also manufacturing challenges, cost challenges and so on, but it's worth it because of the overall purpose. Emily is a living symbol of that purpose.

9. With recent approval in Europe, bluebird bio is seeking approval for LentiGlobin® for Transfusion-Dependent -Thalassaemia in the US next year. bluebird is working toward approval for Lenti-D™ for ALD by 2021, LentiGlobin® for SCD by 2022 and Multiple Myeloma by 2020.

Key Theme 2: A relentless focus on the patient is absolutely foundational.

1. bluebird bio's core purpose is to help patients. The company tries to live that purpose daily.

2. bluebird bio regularly brings in patients and their families to engage in all sorts of ways.

3. It's important to involve patients early and stay connected to the patient. For example, ALD patients provided input into study endpoints that are meaningful for them. Given the grim nature of the condition, having an ALD conversation with a family affected by it is a visceral experience!

4. Nick spends one-third of his time thinking about people, culture, and how to best engage with patient groups.

5. There is a clear focus on investing money in the patient and not on lavish offices or expensive travel. Business travel is always in coach. The company works to exemplify modesty and true patient focus.

6. Leadership in this field requires long term perspective. Quarterly earnings targets are important, but they can't be the exclusive focus. Leadership must not lose sight of the overall purpose of the company and the long-term drivers of success.

Key Theme 3: The next frontier will be overcoming challenges to realize gene therapy's enormous commercial potential.

1. Pricing is a key issue for gene therapies. Nick Leschly has been asked, "How does it feel to have the 2nd most expensive drug in the world?" (Zynteglo). For context, Zynteglo's price is €1.6 million ($1.8 million). Novartis' recent gene therapy for spinal muscular atrophy (SMA) is the most expensive drug in the world, at more than $2 million.

2. Nick's response is that €1.6 million is not the actual price. The 1st up-front payment is €315K. Further annual payments are due over a total of five years, but only if the treatment is—and remains—effective. Every additional payment after the 1st up-front is at risk. And there are many ERTs or equivalent therapies that have very high annual prices that persist for life which, in many cases, far exceed bluebird's or Novartis's recent price. One must compare lifetime patient costs to get a real sense of differences.

3. From a pricing standpoint, bluebird bio wants to establish prices that are sufficient to fund innovation. Two principles that the company follows are:

a. Go at risk – The first payment can be set, but subsequent payments should only be made if the therapy actually works.

b. Cap the upside – Innovation is what really matters, so pricing should be sufficient to fund innovation. However, lifetime caps for individual patients make sense. With a conventional (non-gene) therapy for rare diseases that typically costs between $300K - $600K per year, it's possible to spend $10+ million to treat a patient over the course of his or her life. To avoid situations like that, it's sensible to cap that spend at a certain point (while still providing the therapy to the patient).

4. Over the years, the pharmaceutical industry in general has been subject to criticism about drug prices. A fair amount of this criticism is justified due to regular and unnecessary price increases, in particular in the US (without delivering added value or innovation in many cases). As a result, the trust between companies, payers, regulators, and the public was damaged. That's understandable.

5. Gene therapies are very expensive, so they are subject to scrutiny. However, it's important to remember that pricing is a complicated topic. It's easy to overreact to a high price tag and we must ensure we focus on the value of the treatments in a balanced and multi-stakeholder kind of way.

6. To define the price of a drug, either you base it on comparators—and so are trying to reduce inefficiency in the healthcare system—or you can look at the value to the patients (value-based pricing).

7. A high price isn't necessarily a bad thing, as long as the therapy delivers value that's commensurate with the price. It's important to shift the discussion to the intrinsic value that a (gene) therapy is bringing to patients.

8. For example, the intrinsic value of Zynteglo is huge. It's a sum of the efficacy, added quality of life, avoided complications such as side effects of transfusions, other cost offsets, and so on. Then there's also the direct cost savings (transfusion independence, no need for iron chelators, etc.) which in some geographies amount to ~$2 million.

9. Ultimately, the most successful pricing models in gene therapy will be tied to patient outcomes, adapted for each individual market (while adhering to a general framework), and spread out over multiple years.

10. For this reason, bluebird did not consider cost offsets in setting or justifying their price.

11. A lot of input on pricing came from Europe. Agencies there have been very collaborative.

Key Theme 4: Visionary leadership, risk-taking, and changing current models and mindsets will be key to realizing the promise of gene therapy.

1. bluebird bio—and any other company focused on gene therapies—should keep these ideals and objectives at the forefront:

a. Courage to do the right thing, even when it's the most difficult

b. Keeping patient-centricity as a core focus

c. Driving innovation while finding the right ways to pay for and sustain it

d. Being ready to break the current models to really treat rare diseases

Blue Matter Perspective / Industry Implications:

1. We are living in times of "exponential" change. Pharmaceuticals and healthcare will be significantly affected. After decades in the making, gene therapy is starting to prove its huge transformative potential.

2. With the promise of a cure, one-time gene therapies will have a major impact on patients, payers, and the healthcare system.

3. As of May 2019, there are about 250 late stage gene & cell therapy ongoing studies. The magnitude of that impact will be enormous; it has the potential to transform the classical pharma model.

4. Highly innovative & intensely patient-focused companies such as bluebird bio will be key drivers in changing the system.

5. Visionary and purpose-driven leadership will be critical to overcoming the current barriers to gene therapies reaching their full commercial potential.

6. Pricing and broad patient access will be the key commercial challenges. Innovative players such as bluebird are at the forefront to break and transform the 20th century payer models.

7. After decades of huge efforts with failures and setbacks, gene and cell therapies are finally starting to realize their transformative potential.

8. These are exciting times for innovators and patients. For patients with a rare genetic condition in particular, gene therapy offers great hope as more and more treatments will become reality.

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RARE DISEASES

Passion. Mindset. Experience.

Together, Improving the Lives of Rare Disease Patients.

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