The Breakfast Club "Bottom Line"

Summary of Key Points from the 3rd Blue Matter Breakfast Club™ Meeting

Zug, Skylounge, 5th November 2019

Guest speaker: Theresa Heggie, Senior Vice President and Head of CEMEA, Alnylam Pharmaceuticals

The Breakfast Club meeting of 5th November 2019 included an initial address by Theresa Heggie, Senior Vice President and Head of CEMEA for Alnylam Pharmaceuticals. Following Theresa's address, the broader group engaged in an interactive roundtable discussion and a question and answer session.

The summary below is intended to capture the "bottom line" of the meeting 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.

Building a World-Class Biotech Business in Europe and Beyond: Transitioning from R&D to Commercial and US to International

Key Themes:

1. Alnylam's Journey: A brief overview of the key phases Alnylam ventured through on its journey from its founding to today

2. Alnylam Today: A look at Alnylam's current situation as a world leader in RNAi therapeutics

3. Five Top Tips: Key things learned as Alnylam developed and commercialized a successful product and transitioned from a:

    a. Purely R&D-focused company to one with robust R&D and commercial capabilities

    b. US-focused company to an international / global organization

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:

Dirk Moritz, *Principal*
Rare Diseases Team at Blue Matter
dmoritz@bluematterconsulting.com

Alnylam's Journey

Alnylam's journey can be compared to a three-act play. The company has progressed through two acts and is now in the third:

1. **Science** – Alnylam was founded in 2002 with a vision to turn RNA interference (RNAi), a Nobel-prize winning discovery, into a new class of medicines.

2. **Innovation** – Alnylam made the deliberate and scientifically guided choice to focus on diseases with the highest unmet medical needs. The primary focus settled on rare genetic diseases.

3. **Impact** – Now, the company is working to maximize its impact, investing in Europe and beyond to bring new treatments to the patients who need them.

Alnylam Today

Alnylam is a world leader in RNAi therapeutics and has a strong technology development platform. The company:

1. Operates ~25 sites in 18 countries.

2. Has market approval for ONPATTRO® (patisiran) for hATTR amyloidosis with polyneuropathy in the US, EU, Japan, Canada, and Switzerland.

3. Is developing a robust product portfolio, with 10 programs in clinical development.

4. Has secured solid IP protection (fundamental, delivery, and product-related).

5. Is an industry leader when it comes to partnerships and collaborations, with more than 12 major partnerships with pharmaceutical and biotech companies.

6. Has a ~$10 billion market capitalization and ~$1.7 billion in cash.

Five Top Tips

Top Tip #1: Define the culture before it defines you.

1. It's critical to clearly define the company's vision, mission and core values. These set the tone and direction for everyone in the company and guide its actions.

   a. **Our Vision:** Harnessing a Revolution in Biology for Human Health®

   b. **Our Mission:** Build a top-tier independent biopharmaceutical company focused on RNAi

   c. **Our Core Values:** Commitment to People, Innovation & Discovery, Sense of Urgency, Open Culture, and Passion for Excellence

2. A rapidly-growing company must proactively manage its culture. "If you don't manage the culture, it will manage you."

3. Core values are very important. Key things to remember include:

   a. Everyone should believe in the cause of the organization and remain committed to it through the ups and downs.

   b. Having a set of core values will help manage the culture during rapid expansion.

   c. Senior leadership must set and "live" the culture. Senior management's role in shaping and driving the culture will also help retain the best talent.

   d. Incoming talent should be interviewed against the company's core values.

   e. Differentiation through company culture is possible but not necessary; ownership of culture by every member of the organization—and expression of the culture via external communication—is important.

Top Tip #2: It's all about the people. Build a great leadership team with a business owner mindset and close partnership across geographies.

1. The leadership team needs to adopt a business owner mindset and feel jointly accountable for the overall success of the business.

2. It's important to develop, maintain, and invest in very close partnerships between the global and US organizations (including the heads of regional / local teams and functional departments). Alnylam is a US-based company, and it's key to maintain close connections. The US organization stays informed and educated on the ex-US situation(s), and all areas stay aligned via close, constant communication.

3. Having close partnerships enables Alnylam to better leverage functional and regional expertise in identifying and navigating issues or challenges.

4. Ideally, regional / local and functional heads should be part of the leadership team and take ownership in building a successful business.

5. Find and get the right people. Recruitment into the culture is vital. It truly is all about the people.

6. "Invite everyone to lead!"

Top Tip #3: Build smartly. Create globally aligned, scalable capabilities…and be agile.

1. To deliver a successful product, a company needs more than great data. It needs critical capabilities in a timely manner.

2. There is a host of things to set up including the legal entity or entities, supply chain and local licenses, quality management system, pharmacovigilance, medical information, and many others.

3. Invest time in the beginning on scoping out and prioritizing markets.

4. Create a "Playbook" for office set-up, complete with details about required activities, roles and responsibilities, and other information that will help in setting up an office.

5. Establish scalable capabilities and ensure global alignment. Things developed by global—with the US market perspective--often might not work in Europe & need to be re-developed. Think about global scope from the very beginning!

6. Leverage external teams with experience to help build capabilities.

Top Tip #4: In Europe, focus early on access and engaging with country stakeholders.

1. 1. Outcomes in clinical studies are super-critical for access and you must consider access implications and required outcomes when designing a trial.

2. Key stakeholders such as payers need to be engaged very early. It's vital to introduce the company, technology, and/or product to external stakeholders, understand what's important to them, and ensure clear communication of data.

3. Create an experienced internal access team and partner with local experts.

   a. Incorporate broad capabilities and languages within the team.

   b. Clearly articulate the responsibilities of global, regional, and local market access teams. They need to know who will be accountable for what and how best to work with one another.

4. Continuously engage and educate global colleagues on the complex ex-US pricing and reimbursement process and set / manage expectations.

   a. Benchmark the length of the process by country.

   b. Identify and share pricing analogs.

   c. Provide early input into clinical development and study design to have appropriate data and evidence to clear pricing and reimbursement hurdles.

Top Tip #5: Create trust through senior management engagement and transparency.

1. Create a 'management board', an engagement / governance body.

   a. The body should consist of senior management team members, including R&D.

   b. Communicate a 3-year view of the business to internal stakeholders to set context and allow for planning.

   c. Be transparent about risks and upsides.

   d. Create alignment.

2. Build strong relationships with key internal stakeholders.

   a. Commitment from senior management to build close relationships with regional functional leads is important.

   b. Conduct regular meetings with key stakeholders (functional heads, global colleagues).

   c. Include senior managers in external stakeholder meetings.

Questions and Answers

1. How is Alnylam differentiated against other innovative companies?

   a. We have a "geeky," fun culture, along with a very strong scientific focus. The CEO and leadership have been around for 10-15 years, so there's strong continuity. The whole team just "loves this stuff."

2. When did you start to set up in the EU?

   a. To reduce risk, we started hiring the medical team 2 years before our expected approval and the commercial teams 1 year before.

   b. The majority of our capability build-out was gated to positive clinical trial results. That approach reduced the risk associated with investing in those capabilities. The downside is that it put increased time pressure on the company when preparing for launch.

3. How did you prioritize your countries?

   a. We invested behind high probability revenue in this basic order: US, Germany, France, Switzerland, and Austria. We achieved a considerable benefit rating in Germany, and a price which reflects that value.

   b. Determining expected revenue in each market was important.

   c. Prioritization can also depend on the locations of patients and KOLs.

4. How do you ensure Alnylam stays agile while expanding so fast?

a. We ensure ongoing alignment through face to face meetings and calls. The frequency will depend on the situation and need. Generally, the best practice involves quarterly face-to-face meetings and monthly calls.

b. When things don't move, it's typically caused by misalignment.

c. Monthly launch readiness meetings are critical.

d. Alignment across the leadership team and regular "town hall" style meetings keep everyone up to date and are key success factors.

e. A key learning is to insist that all functions participate in launch readiness meetings so no detail is overlooked

f. "Engage, communicate, and align" is the mantra.

g. You have to be in the details all the time during the set-up phase!

5. Why did you not partner with third party firms in Brazil and Japan?

a. When one is launching a product every year and has the opportunity to leverage investment quickly, partnership might not be ideal. However, it is critical to have good regional market leaders while going for direct presence in countries.

b. Depending on the situation, a combination of direct market presence and partnership is ideal.

6. What are your learnings from ensuring complete alignment?

a. Having a strong business operations team that is tightly connected to all the functional leads allows strong oversight and to consistency in approach across countries.

b. It is also important to have a great business operations head who has an acute attention to detail and a highly collaborative approach. It is important to ensure that all processes run smoothly and efficiently.

7. What has worked especially well at Alnylam?

a. A cohesive leadership team that takes ownership of all elements of the business.

8. What were some key struggles?

a. One of our functional teams decided not to participate in our launch readiness. As a result, we missed key steps, processes were delayed, and we wound up with very tight timelines to be launch ready. Hence, it is important to include all functions to build a holistic launch readiness plan. Sometimes, bringing in external experts to dissect the situation can help you identify where the gaps are in your processes.

b. We also tried to adapt some US-designed standard operating procedures (SOPs) to the EU. That did not work out very well. Better to pause at the beginning to ensure that processes, SOPs, and capabilities are fit for purpose across geographies before finalizing.

Otherwise, time, energy, and money are wasted in retrofitting.

9. How much effort did you spend on disease and technology awareness?

a. We spent quite a lot of effort on both.

b. The amount of effort spent on disease awareness will vary according to market archetype (centralized vs de-centralized) and the rarity of the disease itself.

c. Differentiating on the mechanism of action is important, but clinical outcome is more critical.

10. How can biotech companies with small budgets have smoother and quicker access?

a. Having a value and evidence team in the US (VEST) was and continues to be a key enabler. They collaborated with statisticians and clinical development teams to compile evidence to be used in access across geographies. They understand the data and can identify gaps.

11. What were your key learnings while transitioning from R&D to R&D and Commercial?

a. Engage all key internal stakeholders personally and lead conversations around commercialization.

b. Communicate the key requirements needed to be commercially successful.

c. Educate R&D about commercial needs.

d. As a best practice: Create a business board that regularly meets with all key internal stakeholders.

12. Is there any additional tension in EU vs US?

a. One key aspect is for global teams (if located in the US) to understand the concept and details of rolling launches and market authorizations in the EU. Failure to understand that can cause tension, but we stay pretty tightly aligned.

13. What did you do differently in Alnylam when compared to Shire?

a. We built a holistic leadership team with representations from all functional teams, ensuring broader alignment beyond commercial.

14. Given the choice again in which country would you establish your regional HQ?

a. The main driver is where we find the right talent with the right skills and whose convictions are aligned with our vision, mission, and core values.

15. The company seems more technology centric than patient centric, why?

a. We are committed to be a patient centric organization, but this is more challenging when we are launching into different patient and customer segments with minimal adjacencies.

New Ideas. Better Results.

Blue Matter is a consulting firm serving the life sciences industry. We strive to bring a new approach to consulting with original ideas that deliver a meaningful impact.

blue|matter
RARE DISEASES

Passion. Mindset. Experience.

Together, Improving the Lives of Rare Disease Patients.

George Schmidt
Managing Partner
gschmidt@bluematterconsulting.com

Dirk Moritz
Principal, Rare Diseases
dmoritz@bluematterconsulting.com

Nikos Kontos
Associate Principal, Rare Diseases
nkontos@bluematterconsulting.com

Gary Brandam
Consultant
gbrandam@bluematterconsulting.com

San Francisco
sf@bluematterconsulting.com
400 Oyster Point Blvd.
Suite 309
South San Francisco, CA 94080
650-754-6817

New York
ny@bluematterconsulting.com
575 Lexington Ave.
Suite 24A
New York, NY 10022

London
london@bluematterconsulting.com
5th Floor
14 – 18 Holborn
London EC1N 2LE
United Kingdom

Zurich
zurich@bluematterconsulting.com
Walchestrasse 9
8006 Zurich
Switzerland

Berlin
berlin@bluematterconsulting.com
Potsdamer Platz -
Kemperplatz 1
Berlin Mitte, 10785
Germany

www.bluematterconsulting.com