January 2019

Update Collaboration Models Between Pharma and Biotech

Managing Director Robert Stanislaro of FTI Consulting's Strategic Communications segment moderated a panel discussion in October among select executives from pharma and biotech to provide insight into M&A activity between the two segments. The panel took place toward the end of 2018 at the FierceBiotech 3rd Drug Development Forum in Boston, MA.

MEET THE PANEL:

Moderator:
- **Robert Stanislaro, Managing Director, Strategic Communications, FTI Consulting.**

Biotech Participants:
- **Caroline Stark Beer, VP, Head of Business Development, Alnylam**
- **Thomas Loeser, CFO, Origenis**
- **Debanjan Ray, CFO, CytomX**

Pharma Participant:
- **Joseph Zenkus, Sr. Director, Worldwide Business Development, Pfizer**

ROBERT STANISLARO: Thank you, everyone. I thought I would make some opening comments about the M&A landscape over the last couple of years just to help set the stage for our discussion.

As most you know, 2017 was generally considered to be a lean year for M&A in biotech. There were approximately 101 deals, which compared to about 130 in 2016, and 166 in 2015, which was a record year. If we look at the M&A climate over the first six months in 2018, there was more than $100 billion spent on a variety of different biotech and pharma deals. The year started with a bit of a bang at the JPMorgan healthcare conference as you may recall when Celgene announced a $7 billion deal to acquire Impact Biomedicines.

And then shortly thereafter, Celgene spent about $9 billion to acquire Juno. And there have been several other noteworthy deals throughout the first six months of the year. France-based Sanofi spent $11.6 billion to acquire Bioverativ, which is the Biogen spinout focused on hemophilia.

Sanofi then acquired Ablynx for about $4.8 billion. There have been other several noteworthy deals, as I mentioned previously, such as Takeda's proposed acquisition of Shire. For the remainder of the year, the M&A climate is expected to continue to be relatively healthy especially with the strong balance sheets of a number of our companies in our industry.

With that, we'll open up the panel for a discussion. One of the core considerations around deal making is intellectual property, and as many of you know, IP is the lifeblood of our industry.

ON PROTECTING INTELLECTUAL PROPERTY

ROBERT STANISLARO: Thomas, how do you protect core IP when forming a partnership?

THOMAS LOESER: With Origenis, it's a little bit different because we have a particular focus on small molecule chemistry. So, we start out with filing patents around compound families. And once we enter into any kind of collaboration, we give a license for particular compounds against defined targets and indication areas. Once we move further and we create more data, we then can move on filing our particular selection patents, which then can be assigned to the partner and build up a strong and clean IP position for the partner. This validates at the same time our core IP without compromising it.

ROBERT STANISLARO: Would anyone else like to add?

JOSEPH ZENKUS: I think Thomas is interested in protecting the IP of his company, whereas Pfizer, by the nature of the company, we're frequently on the buy side, so we are looking to gain rights to intellectual property and to be able to exploit that intellectual property.

We recently announced a deal that we did in vaccines, which was with an mRNA [messenger RNA] company. The company had platform technology and had similar concerns around Pfizer using the company's IP outside of the field that we were licensing.

There's a fine line to be sure that the licensee gets the rights that they need to effectively execute what they are trying to do in terms of bringing medicines to patients and ensure that they have the freedom to operate to do so and have the license to do so from the licensor. And that both parties are working consistently with the objective ultimately that the licensor is able to keep the platform IP and use it in licensing in other fields.

Pfizer takes very seriously our role in maintaining confidentiality and working within a partnership explicitly to what we are supposed to be doing. It all begins with the negotiations and how the agreements are drafted, but ultimately, as everybody knows, it ends with how operationally things are put in place. And we put in place specific firewalls to make sure that the IP is protected, and it's not being exploited as it's not supposed to be outside of the field.

ON BUSINESS DEVELOPMENT

ROBERT STANISLARO: We frequently hear about the evolution of a biotech from a research to a development to a commercialization company. Maybe we can start with Debanjan for this question. As a biotech continues to evolve and mature, is there a need for the business development function to also evolve? And if so, how do partnerships change as a company evolves?

DEBANJAN RAY: Great question. Let me describe the CytomX platform first to get some context of this question on how we've thought of our partnering and how our partnership models have evolved. We are a San Francisco headquartered company. We're developing a novel technology that allows us to focus the activity of antibodies, and particularly very potent antibodies to the tumor micro environment. The way we do that is we mask antibodies, and those masks are selectively cleaved off by proteases that are resident in either tumors or other diseased tissue. So it's a novel technology. We got started with this in the 2010 timeframe when there was nobody working on this sort of technology.

So we used business development to advance the company, beef up the balance sheet, and most importantly get additional molecules into the clinic through the power of our partners. As our company has matured, our deal structures have matured as well. When we got started, we were very much a research focused company. We were trying to make this platform technology work. As our CEO likes to say, we were building the plane as we were flying it.

In that sort of structure, the number of deals where we gave some limited access to our technology to our partners, we helped them make these novel molecules. We call them probody. We helped them make the probodies that they were responsible for advancing those probodies through development and ultimately commercialization. And we've seen some of that progression. So one of our foundational partners in these sorts of typical biotech/pharma deals is BMS. We did a broad collaboration with BMS in 2014.

The first asset from that collaboration, which is BMS-986249, a probody, is now in the clinic and has been in the clinic for about the last nine months. We've seen some nice progression and some nice success with those upfront milestones and royalties in terms of collaborations. Over the last several years we have significantly matured our company. So we've gone from a very research platform-focused company to a company that has built a very strong CMC and development function. We've turned the corner to becoming a full-fledged R&D company. And through that transition our deal structures have changed as well.

We've now shifted to doing more risk sharing, profit sharing collaborations where our partners, particularly AbbVie and Amgen, our two most recent partners are trusting CytomX to not only do the research on their molecules, but take them into development, run initial CMC, GMP manufacturing campaigns, and ultimately take these products into the clinic. And that's been a really important evolution for us from a business development perspective because in that role, we control the timelines a lot better.

We have our teams deployed against these projects. Nobody knows the probody platform better than CytomX. And importantly on the backside, we control a significant economic portion of the deals where we have profit splits on the backend. So that's been really driven by the maturation of our company, the maturation of our development team. And the ability for us to convince pharma that not only do we know how to make these molecules, we know how to develop them as well.

Many of those collaborations are turning out quite well. As a matter of fact, the first of those collaborations that we signed with AbbVie, the lead molecule, which CytomX is developing in the collaboration, is now in the clinic. So we've taken an idea and moved it into clinical studies with this more sort of risk sharing/responsibility sharing collaboration.

CAROLINE STARK BEER: I'll add to that. Coming from Alnylam where we've been focused since founding in 2002, [we're] translating the RNAi mechanism into a whole new class of medicines. Our deal history — and I joined in 2008, six years after the company was founded — our deal evolution to some degree actually mirrors what you just described, although I would say it's both a function of the evolution of our company and our strategic needs as well as of course the external environment and the appetite for deals. So early on, deal making was critically important from a few different aspects.

One was providing external validation. Those one to two early deals in a company's lifecycle really send a signal externally to the broader biopharma community that this technology is real, a party has diligenced and decided to move ahead and really invest capital alongside the originator company. And then of course capital, non-dilutive — or not-equity dilutive capital as the other, really primary goal with early deal making.

In the case of Alnylam, and I'll say I joined shortly after this period, we are fortunate in that there was a wave of hope and promise around the technology that enabled deal making, you know, platform deals where we were enabling third parties with IP, and really bringing in significant amounts of capital. And that was really a function of the external environment and appetite. Since then we've seen the next waves of sort of hot technologies go through that same cycle.

As we matured ourselves, similarly and started bringing programs into the clinic, and really refining and honing our strategy, our next wave of deal making tended to be — and both as a function of our own strategy, again, as well external appetite — our next wave of deal making tended to be more focused towards our

product pipeline. But in a way that was complimentary to what our strategic aims were.

With our orphan genetic disease pipeline, which was really the primary focus for a number of years for us, we were very focused on not out-licensing assets that we felt we wanted to retain to develop and ultimately commercialize, but not necessarily globally. So that was where our 2014 Sanofi/Genzyme collaboration came in where we recognized that retaining assets through commercialization was critically important, but that retaining them globally was not necessarily the best way to maximize value.

That offered an opportunity in that case to do a regional deal predominately where for a whole set of our pipeline assets, Sanofi Genzyme had options to regional rights. You know, there are other instances where we've decided that certain therapeutic areas like infectious disease were not places where we were going to build enough heft and expertise to be as successful ourselves. In that instance with our HBV program as an example, we entered into a partnership with a new company, Vir, who is really going to prosecute those programs but where we retain significant downstream rights either to opt back in at 50-50 or of course to participate through milestones and royalties.

Certainly the evolution is still ongoing. As a platform company we are still thinking about partnerships that bring in expertise to allow us to do more with our platform than we're otherwise going to be able to prosecute on our own. And then really the next stage beyond that is how do we start accessing external assets and external technologies.

As a company we're at the early stages of that process. But excited to see where it takes us.

ON UNLOCKING VALUE

ROBERT STANISLARO: That's a good segue into our next question. As everyone knows there are many types of deals, some are simpler in nature, where one company has an asset that another wants, and it's just a matter of figuring out how to share the financial value and transfer the asset.

Others can be highly collaborative in nature where companies seek to advance new assets and there needs to be a broader discussion on how to divide that value. The latter obviously has the potential for greater value creation. Caroline, what do you feel is key to unlocking value, and is there really a sweet spot between the two types of deals that I've just mentioned?

CAROLINE STARK BEER: Certainly we've done, as I said, some global out-licenses. Those have had the benefit of being operationally fairly simple. Typically, Alnylam has driven a program through a certain stage and then there's a handoff point. And that clarity and division of roles and responsibilities has many benefits. The sort of collaboration tax is less, right? Each company knows its lane. And those have been fairly easy to execute and operationalize.

However, as you say, those tend to be more transfers of value rather than new value creation. As a company, we've really thought hard about how you come together with another company, each bring your respective expertise to build something new and then share the value there in a way that the sharing is not going to erode the value creation because we have our experience.

Fifty-fifty co-development and co-commercialization can add a level of complexity that may be really a significant component. And in fact, we — the 2014 Sanofi/Genzyme deal that I mentioned which was predominately regional rights but where we had a few co-co programs — early or I guess late last year into early this year, we actually restructured that deal such that for the set of programs in which we were co-commercializing, we took one, they took the other. We're now paying each other a set of reciprocal royalties on those programs because we felt that taking primary operational responsibility for a given asset really has efficiencies that are important. What we have tried to do is to figure out a way, whether it's doing a multi-asset deal where each party can take a set of assets and take the lead, and then share economics as one model.

Or whether, in the case of Vir, for example, we have a right to opt in to a 50-50 later down the line, but it's really a financial 50-50. It's very clear that Vir will be the operating party. And so really trying to walk that line between both parties coming together, creating something of real value and sharing it, but in such a way that you don't burden the relationship beyond what is necessary to create value. Frankly, it's something that we've talked a lot about and thought a lot about.

I don't know that there's a silver bullet, but I'd love to hear if others have views to add.

DEBANJAN RAY: There's a distinction between what's the economic sharing of the profits and losses and milestones and royalties of a collaboration, and what's the operational sharing. It's very important actually in the deal negotiation process to have honest conversations, both internally and with your external party about what are the strengths of each company.

Where can each company shine in advancing these products to the clinic and ultimately to the commercial space? We've done a lot of this in our most recent deals, as I mentioned our most recent AbbVie deal and our Amgen deal that we signed late last year. CytomX is responsible for advancing these products through essentially clinical proof of concept. And that was abundantly clear in the negotiations process that we've got the capabilities, we've got the infrastructure built.

We're running the machine. We're quite good at it. So we should be the party that does it. Doesn't mean that our partners don't have the opportunity to collaborate with us, give us advice. And, frankly, they've helped us in many of those cases. But also in that negotiation process, we realized that at that stage, we weren't a company that had the infrastructure to do late stage trials until the — as it gets handed over to them for late stage trials. That honesty and self-reflection is quite important as you're negotiating the collaboration.

JOSEPH ZENKUS: Being on the opposite side of the aisle, Pfizer has the luxury of doing transactions across the development

and commercial spectrum and looking at different constructs to operate under in terms of deals. We do deals on the research side, it could be a simple research collaboration. We do co-development deals, we in-license, we externalize, we acquire, etc.

It runs the gamut. The one thing that's consistent in Pfizer's philosophy as it relates to partnering is that we want to listen to our partners. Companies have aspirations to do big things, and if you're not listening to them, as a big pharma partner, then you're doing your company a disservice. It's important because we don't just do one or two deals. We need to respect our partners and make sure that we're a partner of choice.

ON FUNDING AND DEVELOPMENT RISK

ROBERT STANISLARO: So, we've talked about the role of IP, different types of partnerships as a company matures. Obviously, a company has multiple stakeholders to keep happy and take into account their interests. In some cases, investors may have a certain view in terms of the types of partnerships they'd like, companies to pursue. Management may have a different perspective on that. Thomas, how can funding and development risk be better balanced do you believe between companies and their investors?

THOMAS LOESER: That's a very interesting question because before I joined biotech, I was in investment banking. And what we see right now is the third wave of an investment style that started with funding single assets through clinical development followed by asset-centric and build-to-buy approaches. And everybody — and there was about the higher risk-reward portfolio. The second wave was the built to buy structure. The good thing was the early involvement of pharma, but the downside for early stage investors was they have to accept the lower exit price because of the character of the predefined exit.

What we're seeing today, and this is very interesting, is that kind of portfolio-type investing. In the Fifties this was described by Harry Markowitz and he got the Noble Prize for that in 1990, and right now, 25, 30 years later, it's a new style of investing that follows the Markowitz portfolio theory and directs a lot of capital and a lot of non-traditional investors into the sector because when you put together a bunch of low-correlation risk assets, you de-risk the entire portfolio.

But on the other side, you come up, and this is very interesting for financial investors, with some more predictable financial return model. This is why it attracts also in the early stage phase of companies, which is important for us, a lot of interest. This could also give way to new ways of leverage and securitization of such investment stalls.

DEBANJAN RAY: I think about it from three parameters for a company like CytomX. The first is just capital requirements for a company. The second is how you get additional shots on goal for a broad platform like we have. And then third is how do you retain maximal value for the company itself and therefore, for your financial — for your equity investors? Partnering has a key role to play on each of those, and the strategy that we've employed at CytomX over the last seven or eight years from a partnering perspective is, number one, going into this, we knew that building our company would be an expensive endeavor.

Platform company, there was a lot of science to be done and optimization, potential to iteration that needs to be done. And unique to us versus other platform companies is the breadth of our platform. So our probody technology is applicable to really any antibody modality. We can build probody drug conjugates, probody T-cells by specifics, probodies against immunotherapy targets.

And throughout the last seven years, between VC rounds, mezzanine rounds, an IPO and, recently, a follow-on financing, we've stuck to that mix. We've raised about $800 million of capital for CytomX, about half of that has been from equity capital and about half of that has been from field capital. We've received about $425 million in milestones and upfronts over the course of the last several years. So that's checkbox number one. Checkbox number two then is with a platform, you never know what's going to work, and we wanted to have as many shots on goal in the clinic as possible.

Partnering plays a really important role in that because it's much easier to move programs — a number of programs in the clinic if some of those are funded by a partner. Our pipeline today stands at four molecules in the clinic, two of which are wholly-owned and two of which are partnered. Each of those molecules, or all of those molecules, has the opportunity to validate our platform from a clinical perspective. Then step three is how do you maximize value for our company, for our financial stakeholders as we build the company?

Then we made a very conscious decision that we wanted to hold on to our lead programs as long as possible. In other words, as we are having partnership discussions, we made it very clear and very explicit that we weren't willing to partner our lead assets because we wanted to drive the pipelines of those programs. We wanted to communicate data as we felt appropriate, not how our partner felt appropriate. And most importantly, we felt like the way that you build true value for financial investors is to advance wholly-owned programs as far as possible.

We've done that. Out of those four programs we have in the clinic, the two programs or the two furthest advanced are wholly-owned by CytomX, and then the second two are partnered programs. So that's the equation that we set about in 2011, 2012 from a partnering perspective. So far that's really worked well for the company. Ultimately, as the company matures and as we move our wholly-owned programs forward, certainly we will explore partnerships on those assets. But at a position of strength for — and doing the right deal for CytomX for each of those assets. And that's really been driven by the fact that we've been able to hold on to these, use other partnerships to fund our lead programs, and continue advancing them and mature them.

ON MERGING DIFFERENT-SIZED COMPANIES

ROBERT STANISLARO: We have time for two questions. Frequently, you'll have, as we've heard, and as we all know, a

smaller biotech partnering with a larger pharmaceutical company. What do we believe are the most critical elements to ensuring a deal of different sized companies is successful?

JOSEPH ZENKUS: In general, I think culture plays a big component in any deal making process in terms of making sure a collaboration is successful. And even to some extent M&A, depending on the company and the situation.

Getting ahead of things is part of the deal negotiation. As everybody knows, a deal doesn't come together in one day. There's a period of time when the parties negotiate. And during that negotiation depending on the type of collaboration, there's not just the contracts that you're negotiating, but there are plans because you're not going to put together a partnership unless you put together a plan on how you're going to work together, and that plan has to then be executed upon.

What we typically have an alliance management function, and we try to get them involved as early as possible. Well, I try not to get them involved too early because they muck it up sometimes. But you want to get them in early enough so that when the deal is signed the parties are running together to the stated goals of the plan. We like to pre-negotiate plans and transition early. And also termination and effects of termination early because not everything goes to plan.

CAROLINE STARK BEER: The cultural aspect that you started with is what we view to be fairly critical, and you can tell pretty early on in scientific discussions, even before you're negotiating a deal. You can tell pretty early on whether there is a like-mindedness between the teams. Obviously, there's many factors that drive who you ultimately execute a deal with. But certainly, I've noticed that when you have that early meshing, that tends to be the party that we ultimately end up moving ahead with. Of course, you know, you hope that then yields productive relationships.

The other thing we've seen is that multiple relationships we have been part of have started as, smaller, whether single asset or even research collaborations, that's given the companies an opportunity to test the waters at some level to see how strong of a collaborative dynamic we have. And that has ultimately also given us confidence on both sides to take a bigger step to a larger relationship with the knowledge that we've been able to work productively together.

But I also whole-heartedly agree with the more tangible planning aspects and really clear governance. And I also think that the previous comment I made around deal structure and setting things up in a way where you are each playing to your strengths, you're dividing roles and responsibilities in a way that's crisp, all of those things are also critical factors in terms of driving ultimate success in a collaboration.

ON THE IMPORTANCE OF A STEERING COMMMITTEE

ROBERT STANISLARO: Joe, you mentioned Alliance Management teams and when to bring them in. How important do you believe steering committees are, alliance management teams, to ensuring that a partnership moves along according to schedule, and ultimately achieves its goal?

JOSEPH ZENKUS: In my view, governance and steering committees are important, but going back to Caroline's point, it's around culture, right? And it's making sure that there's a sponsor for the program internally at both companies that are seeing eye-to-eye and talking on a regular basis. No matter what governance you have in place, if you don't have the right people on the governance team and ensuring that they're doing the right things on a day-to-day basis, it doesn't matter. It's all about both parties wanting to progress that asset or assets and making sure that they're doing the right things on a day-to-day basis to do so. And then, it must be written into the contract. It's just there in case things fall apart.

At the end of the day you want to be partners with good companies and people that you have similar cultures with and that you trust.

DEBANJAN RAY: Completely agree. The steering committee in the end has a backstop if things don't work. But the real value in the collaboration is the day-to-day interaction between the teams. We think our alliance management function is top notch and incredibly valuable.

And just to add some comments to the last question, an important part of that is anticipating the development of these molecules. If they're veering, then the alliance manager function has to veer along with those molecules. And eventually change the development plan in real time. Just having the right relationships and the right cultural fit between the two companies from that perspective is really important.

ON PRODUCT REIMBURSEMENT

ROBERT STANISLARO: We have time for one last question. In today's day and age, one could argue reimbursement is equally, if not more important, than obtaining FDA approval. How do you determine which company in a partnership is going to take the lead on reimbursement when forming a partnership? How do you determine who's going to be responsible for different milestones throughout a product's evolution [and reimbursement]?

JOSEPH ZENKUS: The commercial partner's going to be responsible for that. There were days back when I was at Mylan on the generic side, you know, that's a different business model? Let's put that aside in the branded innovative space, and Caroline can speak to this because Alnylam recently launched a product. The commercial partner needs to control that entirely. That's something that can't be shared. I've seen litigation and things happen in a nature where you try and have a company that has some type of rights to question the actions of a commercial — the commercial partner.

For example, could the commercial partner be bundling it with other assets and using it as a loss leader which, then if I was giving profit sharing to my friend here, they would be kind of out of luck because I'm using this as a loss leader to drive other profits for Pfizer, and they're getting the short end of the stick. Well, that's typically — you solve that in the contract, but no way is Pfizer going

to say okay, Alnylam, we're going to control the pricing and the reimbursement decisions.

But you can have a say on that, and, you know, and we'll listen to what you say, and we'll use commercially reasonable efforts to listen to what you say. And that's just not going to work. You invest with a company like Pfizer because of our commercial capabilities and to drive that. Not to kind of have a joint decision on how you price or look to get reimbursement. At least that's my view. That doesn't work.

ROBERT STANISLARO: We're out of time, so thank you, again, to our panelists.

Panel comments have been condensed and edited for clarity.