

# Brett Monia CEO, Ionis Pharmaceuticals

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*Dr Brett Monia, co-founder and CEO of RNA therapeutics pioneer Ionis Pharmaceuticals, outlines the company’s extremely promising development pipeline, commercial partnerships with Big Pharma, and his ambitious strategy to launch ten or more products by 2025.*

**Brett, having been one of the co-founders of Ionis Pharmaceuticals in 1989, could you provide a brief overview of your journey with Ionis over the past three decades?**

My training is in drug discovery and development, so my career goal has always ultimately been to discover, develop and deliver drugs to patients. I completed a PhD in Pharmacology at the University of Pennsylvania and subsequently completed a postdoc in molecular pharmacology at what was then SmithKline & French Laboratories, before being recruited to help create Ionis in 1989 as a founding scientist. Actually, when the company was created, it was named Isis Pharmaceuticals but in 2015, we changed our name to Ionis Pharmaceuticals for obvious reasons.

I ran our drug discovery group in expanding capacities for decades and I am proud of the fact that today Ionis boasts a stunning pipeline of over 40 drugs in clinical development, along with three products on the market (commercialised through our partners). My career over the past three decades with Ionis has been an exciting one, as I took on expanded roles in drug discovery and development, oversaw some of our Phase III programs, and broadened more into the business side

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of the company. I became COO and SVP of Translational Medicine in 2018 and as of January 2020, I am now CEO of Ionis, following the stepping down of our founding CEO, Dr Stanley T Croke, who is now executive chairman.

Fundamentally, Ionis is a science and drug development driven organization. Science and innovation are at the core of the company. This was a major factor behind my appointment: the Board recognized that it would not be an easy task for someone to take over the mantle of a founding CEO that had been with the company 30 years. It was of paramount importance that the new CEO really understood the cutting-edge science and innovation behind our platform and products, and more importantly, the culture of innovation within the organization that places patients at the centre. Therefore, while there were external and also other internal candidates, the Board concluded fairly quickly and unanimously that I was the best choice for the position.

### **What are your top priorities on your agenda for Ionis as the new CEO?**

I am extremely excited about Ionis's current positioning. We have built tremendous momentum over the past few years and we are on the verge of great achievements that will take us to the next level. Our antisense drug discovery platform, whose development and clinical validation I was intimately involved in, has generated a broad pipeline of exciting candidates. We have many programs currently in Phase III development. All these medicines are potentially transformative in nature. These are not "me too" drugs that aim to provide incremental value. We are talking about hugely exciting, first-in-class or best-in-class, potential blockbusters.

Looking forward, we are now preparing to deliver many of these compounds to the market for a number of different indications. Some of the indications are for rare or ultra-rare diseases but we also have assets targeting large indications in areas like cardiovascular diseases that affect millions of patients.

Over the past few years, we have developed many strategic partnerships with large pharma companies like Roche, AstraZeneca, Novartis, Pfizer and Biogen. There is a tremendous appetite within the industry for collaborations with Ionis Pharma because of the uniqueness and efficiency of our drug discovery platform. We have now reached the point where we can be very selective in our partnerships. The companies we partner and work with are those we believe can commercialize our products most efficiently so that they reach as many patients as quickly as possible.

In addition, now that Ionis is in such a strong position in terms of our robust pipeline, validated platform technology, strategic partnerships, and finances, one of my priorities over the next few years is to build our own pipeline and create our own commercial capabilities. This will be our own portfolio, which we will bring to the market ourselves. We plan to focus our efforts here in rare diseases.

Overall, I have set us the ambitious goal to launch ten or more products through 2025.

### **Ionis is the pioneer in RNA therapeutics. Can you share a little more on this platform?**

The genesis of Ionis was our shared frustrations in the inefficiency of the pharmaceutical industry in the late-1980s and their inability to deliver drugs that addressed real patient needs. Between us, we had a lot of experience in the pharma industry and so we understood the benefits as well as the limitations of traditional drug R&D platforms. Around that time, some seminal publications came out,

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suggesting that a technology referred to as antisense could potentially be a new method of drug discovery. The publications were very academic in nature but in principle, it looked like it had the potential to form a new drug discovery platform. That really excited us, and we decided to create Ionis to explore this new technology.

Most drugs on the market today, whether small or large molecule, primarily target proteins, aiming to affect their functions in various ways. Our antisense platform targets RNA instead. RNA is the genetic code for protein synthesis, so we are intervening earlier. We develop drugs that bind precisely to messenger RNA in our body to prevent the creation of a disease-causing protein. Our platform technology has now been clinically validated and we have shown that our platform offers tremendous advantages in terms of efficiency and speed. It explains how a small company like Ionis we currently have 500 people can have a pipeline of 40+ assets. The most important advantage, however, is that the platform allows us to target and tackle diseases or indications that were previously thought to be "undruggable" or unapproachable using traditional drug discovery platforms. We are talking about conditions like Huntington's disease, amyotrophic lateral sclerosis (ALS) and many others, particularly within the neurology space.

What is also very exciting is that antisense therapies can be administered in many different ways, from oral to IV to intradermal to subcutaneous and so on. This means that they can reach targeted parts of the body and minimize drug exposure in other parts, providing improved safety.

Through our efforts on this technology, we have pioneered a new industry segment focusing on RNA therapeutics. Today, there are many other companies following in our footsteps, but we led the way to develop and prove that this technology could work, and we continue to lead today.

### **Could you tell us more about your commercial partnerships with Big Pharma?**

Our overall focus is in areas with major unmet medical needs. Our two largest franchises currently are in neurological diseases and cardiovascular and metabolic diseases. We have over ten drugs in each of these franchises, with more coming. So far, clinical data suggest that our drugs work very well.

Generally, our commercial partnerships today provide global commercial rights to our partners. Our partners the likes of Roche, AstraZeneca, Novartis, etc. have the global muscle to launch our products in the largest markets like the US, EU, Japan, and China. Just last year, we concluded such an agreement for a Phase II drug with Pfizer through our majority-owned affiliate, Akcea Therapeutics, for a global exclusive licensing agreement for certain cardiovascular and metabolic indications.

We will continue to partner strategically with Big Pharma players for our assets in broad indications.

### **How prepared is Ionis to develop and commercialize its own pipeline of products?**

I think we have built a very strong foundation. In addition to the inherent novelty and value of our platform technology, our platform has also allowed us to leverage economies of scale. Our process of drug R&D is essentially the same from one drug to another, so each drug we discover teaches us something that we can then apply to the next one, and so on and so forth. In addition, we have a clear picture in terms of the manufacturing cost of goods and all the other aspects that go into commercializing a compound.

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Since our platform is novel, over the past few years, we have also developed strong regulatory relationships with global regulators like the US FDA, the EMA, the Japanese PMDA, and increasingly, the Chinese NMPA. This is important because we have to work with them to educate them on the new technology as well as to understand and meet their specific clinical trial and other regulatory requirements.

I think we can see that RNA therapeutics is growing in popularity and we do see that the playing field is becoming more competitive. New biotechs have been established, and also, large pharma companies are building antisense capabilities internally because they recognize that this is the future of drug R&D. But we are the pioneers – we created this space – and we have been working on this technology for 30 years. We have secured the relevant IP across all aspects of our technology, including the foundational medicinal chemistry of our drugs, as appropriate. Beyond that, we also have extensive corporate knowledge about drug targets, molecules, manufacturing processes and other elements of the drug R&D process, which may not be patentable but is infinitely valuable. Of course, we are also continuously innovating. We are not simply resting on our laurels and using old technology. We create new IP and generate new insights every year. This is why it has been very hard for newcomers to break into this field. Many companies find that it is simply easier to work with us in this space rather than reinventing the wheel, and this is also how we have established so many strategic partnerships.

In terms of other considerations, such as pricing and reimbursement, looking at our products today that have been managed by our partners, they are performing well. Our drugs are novel therapies with transformational therapeutic value, they are not “me too” drugs and they will not be the third or fourth or fifth drug on the market for a specific indication. We will have to evaluate when we get to that stage, of course, but I do not anticipate that our products will face the types of reimbursement or pricing challenges that drugs more focused on incremental benefits have had. We will also do our best to ensure that patients have access to our drugs that need our drugs.

As we are not a Roche-sized company, we want to manage our growth appropriately. We want to grow in proportion with our culture and our science. We already have over 10 drugs in our Lonis-own pipeline for various rare diseases. A high priority for us is neurologic rare diseases, so we will continue to invest in this space.

### **How will Lonis’s transformation into a commercial organization influence the core of R&D and science that you highlighted previously?**

Our top priority is to insulate our commercial activities from our scientific and innovative activities. We are committed to our cutting-edge science and culture of innovation, and our commercial activities will not compromise that commitment.

For the moment, we are still looking at multiple strategies, whether it is build (i.e., create) or buy (i.e., partner), or a hybrid of the two. We anticipate that the first drug from our Lonis-owned pipeline will be ready for the market in three years, so we have time to build our commercial strategy.

### **Looking forward, what can we expect from Lonis in three years?**

Certainly, the company will look quite different! Firstly, today we have three drugs on the market. In a few years, we want to have over ten drugs on the market. We are excited to launch our products for areas of severe unmet medical needs like Huntington’s disease, ALS, Prion diseases, and others.

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This will have a huge impact on the industry.

As mentioned, in three years, we also plan to have firmly established our commercialization strategy and launch the first product resulting from this strategy from our Ionis-owned pipeline. By that time, our commercial capabilities should be firmly established.

Thirdly, we are always looking for and investing in new technologies and platforms to enhance our drug R&D capabilities. We do not want to be a one-platform company. Of course, these investments will be complementary to our antisense technology. Our deep expertise in RNA biology and therapeutics is second to none so we want to continue expanding our scope in this field.

Ultimately, today we are the global leaders in RNA therapeutics. 30 years ago, we had a dream that antisense technology could change the way drug discovery is done and deliver innovative drugs to patients with severe unmet needs. Today, we are delivering on that dream. We have built the most efficient drug discovery platform in the industry and we are leading the charge. I want Ionis Pharma to have an even greater impact on the industry moving forward. Everything we are doing has brought and will continue to bring tremendous near- and long-term benefits to patients, who are at the core of our mission. We want to continue to deliver on our dream.

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