Joe Wiley
Chief Executive Officer
Amryt Pharma

Joe Wiley, CEO, founded Amryt and is a non-executive director of NASDAQ listed Innocoll AG. Mr. Wiley has over 20 years of experience in the pharmaceutical, medical and venture capital industries. Mr Wiley opened and led Sofinnova Ventures' European office.

AMRYT PHARMA

Amryt Pharma is a specialty pharmaceutical company focused on the developing and delivering innovative new treatments to help improve the lives of patients with rare and orphan diseases.

Amryt's lead product, Episalvan®, received marketing approval for the treatment of partial-thickness wounds from the European Commission in Issue 10 | 2016. Amryt intends to further develop Episalvan® as a new treatment for a hereditary skin disorder called Epidermolysis Bullosa in both Europe and the US.

ENLARGED AMRYT PHARMA JOINS AIM AFTER REVERSE TAKEOVER

B&M: Joe Wiley, CEO of Amryt Pharma, please could you start with telling us your elevator pitch?

JW: Amryt is a new pharmaceutical company, set-up in August 2015. We develop drugs for orphan indications, meaning rare diseases. The business was setup initially to acquire assets in the orphan disease space. We recently acquired two companies with promising orphan drug candidates; Birkin, which is based in Germany and Som, which is based in Switzerland. Through these two acquisitions we have a pipeline of products.

We believe our lead product, Episalvan®, which is in late stage development for a rare, hereditary skin disorder called Epidermolysis Bullosa (EB), has been meaningfully de-risked following its European approval earlier this year for the treatment of Partial Thickness Wounds (PTWs). Episalvan® is expected to be launched in PTWs in late 2016, where it will represent a new category of advanced wound care management, a market worth in excess of €150 million.

We also have a promising pipeline of earlier stage orphan products and benefit from sales of our dermacosmetic product line, Imlan. We believe the combination of our sustainable core business with the significant potential upside of our orphan portfolio provides investors with an attractive risk/reward profile. We recently joined AIM and Dublin's ESM following the reverse takeover of Fastnet Equity PLC, where we also raised £10m to accelerate the development of Episalvan® in EB.

B&M: When you say market authorisation, you have moved on from orphan designation to full approval?

JW: We have. On average it takes around 14 years and over a billion dollars to develop a pharmaceutical through to approval. There is a high attrition rate in pharmaceutical drug development – many drugs never make it.

Episalvan®, has already gone through a full programme of preclinical, clinical and multiple phase 3 trials, and even gone through the EMA and been approved for marketing in partial thickness wounds in adults. We are very far down the road and already at the commercialisation stage.

We are currently also developing our lead orphan drug in an orphan indication called EB. It has currently been approved for the treatment

of partial thickness wounds in adults. Partial thickness wounds are wounds that don't go all the way through the skin. As opposed to full thickness wounds that reach beyond the skin into the muscle and underlying tissue. Partial thickness wounds heal very differently from full thickness wounds. The skin layer is damaged but left intact, and healing is through residual satellites in the wound bed differentiating and migrating across to close the wound. Our product accelerates that process of differentiation and migration of the keratinocytes that closes and heals the wound.

It is interesting that Episalvan®, works regardless of the aetiology of the wound. We have done phase 3 studies in grade two burns and in split thickness donor site wounds, and it works beautifully for both thermal and mechanical wounds. For example, when a surgeon scrapes off a layer of skin to transplant elsewhere, a partial thickness wound is created on the donor site and the product works just as well in these sorts of wounds. We have also done a proof of concept study in a rare disease called Epidermolysis bullosa (EB). EB is a rare and distressing genetic skin disorder affecting young children for which there is currently no treatment. In EB, skin is easily damaged through slight trauma. EB is caused by an underlying genetic defect that affects the proteins which hold the skin down, making it very friable. It is known as "butterfly skin", like the wings on a butterfly. The wounds resulting from this condition are partial thickness wounds, and our product has shown in clinical studies to accelerate healing. We have approval in Europe to bring the product into a phase 3 or pivotal study in EB sufferers. By mid 2019, we are hoping that the drug will be available to treat patients with this rare and debilitating condition.

B&M: From a strategic point of view, you mentioned you acquired the two assets you have. Is that the approach you will continue to take - to acquire assets to build the portfolio rather than R&D?

JW: Right now we've acquired a pipeline of exciting products and we've raised the money to develop those products. We're not actively out there looking to acquire any other products or companies at the moment.

At present we are focussed on commercialising our lead asset, developing that same product in a phase 3 in EB and developing our fantastic team. Our other products will also go through the same process in time.

Apart from our lead asset, Episalvan®, we also acquired another product from Birkin called Imlan. This was the first product Birkin developed and uses the same API as Episalvan® but in a different concentration and different formulation. It is sold as a cosmeceutical and does c. €1 million in sales right now.

We do not necessarily want to be in that space, but the product is really interesting and the data is really good. We are looking at developing it for a more medicinal purpose, and hopefully will increase sales of that product as well.

In addition to these two products, we also have another product still in preclinical stages, which we will bring forward in time.

B&M: Is your preclinical product also an orphan drug?

JW: It's a drug to treat orphan conditions, although it doesn't have orphan status yet. Orphan designation, or orphan approval, is often applied for at a later stage. AP102 is a somatostatin analogue,

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and it is used in the treatment of two conditions, possibly three. We are focussing on Acromegaly, which is an overproduction of Growth Hormone, from a tumour in the pituitary gland. You get big hands, a big forehead, big jaw, and also a hypertension, cardiovascular disease, diabetes and other systemic issues. Acromegaly causes a two-times increase in mortality risk. The treatment of choice for patients is surgery to remove the pituitary tumour, which is effective in about 50% of cases. In the other 50%, they need to be treated medically.

Alan Harris, the founder of Som, which we have acquired, was involved in developing a therapy for these surgery-resistant patients with Acromegaly when he was at Novartis. The product is called Octreotide, which is now a 1.65 billion dollar product. So, within the cohort of patients who have failed surgical treatment, most of them are on Octreotide or another product called Ianreotide. These are both somatostatin analogues, and will work fully in roughly 30% of patients who try them. The remaining 70% need an alternate treatment. Novartis realised this, as did Pfizer, and developed other products. Novartis brought a product called Pasireotide, and Pfizer brought a product called Pegvisomant. Pegvisomant is a growth hormone receptor antibody. It acts as an antagonist, blocking the receptor and reducing the action of growth hormone. There are two problems with growth hormone receptor antagonists – the first is that it has no effect on the tumour size, only on the action of growth hormone. Secondly, it has a tendency to elevate liver enzymes.

Pasireotide, however, is a somatostatin analogue, so it does have an effect on the tumour. It binds to somatostatin receptors two and five. Octreotide only binds to receptor 2. Pasireotide is clinically effective, but it can cause diabetes as a side effect.

Alan set up Som Pharmaceuticals to develop a new somatostatin analogue. He wanted to find a product as effective as pasireotide, that did not cause diabetes. Our preclinical work has shown that is exactly the profile our AP102 drug candidate has. We now have the opportunity to bring the product into clinical trials and demonstrate its results in humans. If successful, it could be a fantastic new drug in the arsenal of physicians.

B&M: What do you think is so attractive about the orphan disease market?

JW: Orphan diseases affect small numbers of patients. By US definition, it is less than 200 000 patients, and less than 250 000 in the EU. In the past, pharma did not develop drugs for these diseases because with such small numbers of patients, they struggled with getting a return on investment. However, the Orphan Drug Act in the US in 1983 created incentives to develop orphan drugs. Japan and then Europe followed suit in 2000.

The biggest incentive is market exclusivity. If you develop a product in an orphan indication and get orphan designation, you get seven years market exclusivity for your product in the US, outside of any IP you have. In Europe, you get 10 years market exclusivity.
There is generally a large unmet need in orphan disease treatments. So the bars to approval tend to be lower. The studies do not need to recruit as many patients as in other indications and hence the costs of doing these trials are lower.

Finally, for a small company like ours, commercialisation is a simpler process. I could never develop a product in a condition like hypertension, for example, where

I would have to go to every single general physician in every country to promote my product. That is not tenable for a small company. In rare diseases, however, there are a few highly specialised key opinion leaders in specialised centres for each condition. It is therefore possible for a company like Amryt to develop the relationships required to get our products known, and supported by those key opinion makers. In EB, for example, there are only 15 treatment centres in the US. We only have to target these 15 centres and we have captured the entire US market.

B&M: What does the risk reward outlook look like for Amryt?

JW: We feel that the EMA approval was a huge de-risking factor for us as a company. There are very few drug development companies of our scale that have an approved product. This means that one of the two biggest regulatory agencies in the world is happy with the efficacy of Episalvan®, the safety profile, and also the quality and manufacturing. For Episalvan® in Europe, the major hurdles have all been passed. The only remaining risk is commercialisation, and we have a really strong commercial team and Board.

The bigger market opportunities for Episalvan® is in developing it in EB for which we are currently planning a phase III study. In Europe, the product is already well known by the regulatory agency. We do have to fully engage with the FDA as well, with which we have had much less interaction with to date.

Of course there is still risk, because we are yet to prove efficacy in EB patients in a large enough study. However we feel that our wealth of data in non-EB indications, the consistency of findings, and our successful proof of concept study in EB meaningfully de-risks our programme.

B&M: You recently secured £10 million in funds. What do you plan to do with the money?

JW: First of all, there was a milestone payment to the Birkin sellers that we satisfied.
Secondly, we are in the planning stage now of bringing Episalvan® forward in phase 3 for the EB indication. We aim to treat the first patient in early 2017. This is our main focus.
In addition, there is working capital, and some work we need to do with the Som product as well.
We have assembled a great management team. Rory Nealon is our CFO and COO. He is an accountant by training but spent the last 12 years working for a NASDAQ listed business called Trinity Biotech. During that time he did 12 acquisitions and integrated 12 businesses, including manufacturing facilities, like we have done with the Birkin acquisition.

We also have Michele Bellandi, who joined us from running Shire Europe – a 1.1 billion dollar business with 600 odd employees reporting to him. He shares our vision to become a leading player in the orphan disease space.

At the Board level, our Chairman Harry Stratford was the founder of Shire, the largest orphan disease company with the Baxalta deal, . We also have Ray Stafford, who developed the well-known product Sudocrem, and Cathal Friel, executive chairman of Fastnet Equity. He is a shareholder and remained on the Board. Finally we have James Culverwell, who was the top rated biotech and pharma analyst in the City of London for many years. He headed up Meryl Lynch's European group.
We have built a Board and team that one would expect from a much larger company, which we assembled because we know where we want to be headed. We plan to further strengthen our team in the near future and we are in active discussion at the moment with a potential Chief Medical Officer.

B&M: Could you summarise your next key milestones?

JW: With regards to the team, we are in the final stages of bringing in our scientific advisory board together, with some world leading experts joining us.

In terms of the products themselves, we are engaging with both EMA and FDA to get Episalvan® through phase 3 in the EB indication. And with regards to commercialisation, we are looking at various strategic options. EMA approval opens up Europe as well as other parts of the globe, as many countries accept EMA approval. We are working with potential partners in various geographies as potential distributors or to license our products.

In Europe, we are working on developing Imlan, the revenue generating dermo-cosmetic product to potentially reposition it as a medicinal product.
In addition we're developing the necessary programmes to hopefully obtain t orphan status for our Acromegaly candidate AP102 in the next number of months as well.

B&M: How would you describe your level of ambition for Amryt?

JW: We want to be a leading player in orphan and rare diseases. We have the capability, the team, and a fantastic cohort of assets. Ultimately we will be bringing in other assets in time, but that is not the near term goal. ■

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