Interview: Annie Hubert – Senior Director, EU Section and Public Policy, Alliance for Regenerative Medicine (ARM)

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Annie Hubert, Senior Director, EU Section & Public Policy for the Alliance for Regenerative Medicine (ARM) describes some of the issues that companies in the advanced therapies field are facing in terms of market access and stakeholder education in Europe, as well as some of the key breakthroughs that European companies have made in this dynamic sector.

Could you begin by giving us a short introduction to your background?

I am a pharmacist by education and have always worked in the industry in different areas; in regulatory affairs, pricing and reimbursement, and more generally corporate affairs. I spent more than 10 years at Amgen and my last position there was as head of European public affairs.

I wanted to step back from the big company environment; the Amgen that I joined was very different to the Amgen that I left! I really missed being part of a small, agile company that has to do a little bit of everything and wanted to work in that kind of environment again. Therefore, I started my own consultancy, with an objective to help SMEs in the advanced therapy field. I am Belgian and the sector was vibrant at the time in the country, with between five and seven very dynamic SMEs developing advanced therapies. This is how I started to work for the sector. There were a few company issues specific to Belgium, such as navigating the complexity of the national

implementation of some European directives, so my task there was trying to improve the operating environment for them.

To do so, I created a coalition to bring together companies working on advanced therapies in Belgium, in order to be able to represent them and have an advocacy platform to help address their key common issues.

How did you come to your current position at ARM?

When I first started as a consultant for the Alliance for Regenerative Medicine, there were two separate organizations: ARM in the US and a sister organization in Europe, the Alliance for Advanced Therapies (AAT).

They asked me to help with a specific project; namely, setting up the first Advanced Therapy Investor Day in Europe, which took place in Brussels in 2013. There had been similar events organized by ARM in the US, but nothing at that point in Europe.

This was my first collaboration with AAT, which later merged membership with ARM with the mission of becoming a global organization specializing in advanced therapies. I now work for ARM, representing the Alliance's European section.

What are ARM's current priorities in Europe?

Market access is a big priority for the organization as a whole and this is also true in Europe. In Europe, you do not have one system, but 28+ different markets and frameworks. There are some initiatives to increase cross-border collaboration in Health Technology Assessment (HTA) and scientific advice, but every country is different, making it very complicated for companies that do not necessarily have a lot of resources with local know-how. This complication is compounded if a company has a highly innovative and potentially disruptive product.

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There are many regulatory challenges as well, but in general, we can say that the regulatory authorities are very supportive, open to dialogue, and ready to take a flexible approach to address the multiplicity of specific difficulties of ATMP development, without lowering the safety and efficacy standards in their assessments. Payers however, are still somewhat uncertain of these new

technologies. More dialogue with them should be a priority in order to make sure that products with marketing authorisation are made available to those who need them.

The European Medicines Agency (EMA) is now creating a separate department for advanced therapies; emulating a move already made by the Japanese. How would you characterize the level of support that your industry receives from regulatory authorities?

The EMA is very supportive and has taken a proactive approach in identifying solutions to foster sector development in Europe and, in some cases, allow early patient access to innovative treatments. Frameworks like PRIME (PRIority MEdicine), an EMA scheme to enhance support for the development of medicines that target an unmet medical need, is particularly relevant for advanced therapies; about half of the medicines under PRIME are Advanced Therapy Medicinal Products (AMTPs). The authorities are conscious of the benefits that our industry can bring and dedicated to helping find solutions to the unique issues we face.

In addition, there was a realisation that is not useful to have early approval if the product cannot be put on the market because the data generated do not fit the requirements for HTA assessment and payers. Therefore, for several years now, there have been initiatives to try and engage the HTA bodies and payers in Europe at a much earlier stage, i.e. product development. Scientific advice is available to member states' HTA bodies at the same time as regulatory advice and HTA bodies from different countries can participate, engage in dialogue and provide joint advice. The idea is to have a consolidated approach to clinical development and satisfy the regulatory, safety, and efficacy requirements of the regulatory authorities, as well as the value assessment by HTA and reimbursement bodies.

Advanced therapies are extremely costly to develop and reimburse. Can a democratic approach to introducing these therapies across all of the 28 EU member states work, or do more developed countries, which might be better equipped to absorb the costs, have to come first?

The pricing issue is not specific to advanced therapies, but to all products that are costly to manufacture and develop. The specificities of advanced therapies include the fact that they are potentially curative, or have a long-term, durable effect, which at time of approval may not be fully assessed due to a lack of long-term data. These are aspects that need to be evaluated differently from other products. Pricing is obviously of high concern to the payers within Europe but overly focusing on a product's price tag is not a good approach. We should rather take a more holistic

view and try to assess the value of the product overall by considering its positive impact on the patients, their caregivers and families, healthcare systems, and society. This could also include more innovative ways to pay for the product; for example, outcome-based payment models or annuity payments, as the treatments have the potential to be effective for the rest of the patient's life.

Which countries in Europe are taking the lead in fostering this more holistic approach to regenerative medicine?

The UK NICE has run a mock assessment of an AMTP with the conclusion was that their process was fit for purpose and that the system was ready to evaluate new payment models. In that aspect, the UK has taken the lead within Europe, but I think most countries are still very uncertain about what is required. The UK NICE approach also shows clear limitations as it makes recommendations exclusively on the basis of their cost-effectiveness analysis. We know that several countries have started a reflection process to define how to handle ATMPs but, so far, I have not seen a clear outcome from these meetings.

What are the competitive advantages of Europe compared to the US? Does the fact that EU countries generally have a single payer work to the region's advantage?

There are many countries in Europe with a single payer, but others, including the big ones, require negotiations at regional levels. For instance, there are 17 autonomous regions in Spain requiring 17 separate negotiations for funding in addition to the price negotiation at national level. In addition, approval from a single payer does not necessarily guarantee market access. With 28 member states with different systems, there are a lot of other layers to consider, for example, convincing hospitals of adopting the products. Hospitals would have to make sure that they have systems and personnel in place to be able to handle and administer the products, meaning that getting the product to the patients will be a gradual process, not one solved overnight by reimbursement approval, although that is a significant step.

Which companies does ARM in Europe represent?

About 20 percent of ARM members are based in Europe. ARM mainly operates in Europe through its EU Section and two European-focused Committees: one Regulatory Affairs and one on Reimbursement. Any ARM member, regardless of whether the organisation has European operations, can participate in these committees. Most of our European members participate in these committees but we also have a large proportion of US-based participants, as most companies want to operate internationally. .

Which are the key European companies in this sector?

People tend to forget that Europe has historically taken the lead on AMTPs; the first approvals with high scientific and regulatory standards came from Europe and from European-based companies. The very first was a product from TiGenix, a Belgium-based company; others include products from UniQure, a Dutch company, from Chiesi and Italy's Molmed, and from GSK. Additionally, three US companies have also had product approvals in Europe: Janssen, Genzyme, and Amgen.

In the US, too, the first gene therapy product ever approved by the FDA, Kymriah, is a product from Novartis, a Swiss company.

I sometimes hear disappointment that these products do not live up to their expectations and are not commercially attractive, but these products and their respective approvals represent major scientific and healthcare advances and serve very different disease areas, with completely new approaches. The fact that Europe has been able to approve these products with high scientific standards has laid the groundwork for the truly transformative products to come in the future.

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The European companies with approved products on the market represent a diverse cross-section of the life sciences sector: from Big Pharma players like GSK to family-owned companies like Chiesi. What does this say to you about the European mindset?

The level of innovation in the European pharmaceutical sector has always been very high. The quality of research by academic centres is strong and technology transfer from academia to industry via spin-offs tends to be very successful, even with limited resources. This is also a big difference between the US and Europe: companies in Europe often have to make do with very little money; the difference in market capitalizations of new US companies versus new European companies is generally quite significant, yet these European companies have still been able to bring products to market.

The fact that large pharma companies are now demonstrating their interest and investing in the field is an indication that the sector has gained in maturity and attractiveness.

What is ARM working on currently in Europe?

We have just published a position paper with a series of proposals to facilitate approvals for clinical trials with gene therapies in Europe. These products face specific difficulties as they have to comply with the GMO legislation in addition to the traditional requirements for medicinal products We have liaised with trade organizations and the paper has been issued in conjunction with them.

What are your expectations for ARM's Cell & Gene Meeting on the Mesa, to be held in October 2017 in La Jolla, California?

This is a great opportunity to assess the progress in the field in general. It will be possible to see how companies in our field are progressing from one year to the next and there will also be a series of interesting panels on market access, clinical and commercial progress and manufacturing, among other topics. European companies are well represented, but unfortunately because of the travel distance, it is not easy to attract many European public officials to this meeting. Most of all, it is an opportunity for me to meet with our global membership, to try and understand the issues they are experiencing, and exchange ideas and proposals regarding ways ARM can support their efforts and the sector overall.

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