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Restructuring for Biopharmaceutical Success

Merck Serono fuels innovation with an integrated research, development, and manufacturing program and seed funding for startups.

RITA PETERS, EDITORIAL DIRECTOR

Innovation in biopharmaceutical development is typically associated with startups, not a company with nearly 350 years of history behind it. When faced with a corporate restructuring, Merck Serono, the biopharmaceutical division of Merck KGaA, took some innovative measures to refocus its research, development, and manufacturing efforts to accelerate biopharmaceutical development.

Merck KGaA (Darmstadt, Germany), the oldest chemical and pharmaceutical company in the world, was founded in 1668 when Friedrich Jacob Merck acquired the Angel Pharmacy. Merck Serono was formed in January 2007, when Merck KGaA acquired

Serono S.A. and combined it with the former Merck Ethicals division. The global biopharmaceutical company develops both chemical- and biological-based prescription drugs to treat cancer, infertility, growth disorders, cardiovascular, and metabolic diseases. Products are marketed in more than 150 countries.

EMD Serono is the company's subsidiary in the United States and Canada. Combined, Merck Serono and EMD Serono have 15,600 employees worldwide, with 2012 revenues of €6.4 billion (\$8.67 billion). EMD Serono, headquartered in Rockland, Mass., employs more than 1100 people in the United States; over 700 are based in Massachusetts.

In early 2012, Merck KGaA announced a restructuring, including the closure of the Serono headquarters in Geneva, Switzerland and elimination of 1000 positions. The transition strategy included seed money for spinoff companies to continue research originated at Merck Serono, a new headquarters in Darmstadt, and centralized R&D efforts in the US.

“At Merck Serono, we spent the last couple of years really thinking hard about how to refocus our pipeline and to reprioritize our pipeline, in particular to advance and accelerate the mid- and late-stage pipeline. At the moment, we have a very strong focus on oncology,” says Annalisa Jenkins, executive vice-president, head of global research & development for Merck Serono. Currently, the company has 16 projects in various stages of clinical development.

Other R&D efforts focus on immuno-oncology, immunology, and neurology. “Across the board, we believe in a strong focus on translational medicine and improvements in our understanding of biology to really focus on this area of personalized medicines. Each one of our research programs is accompanied by a biomarker approach,” she says.

REINVENTING R&D

“We recently announced that we would be putting all R&D back together again so that we could really focus on a fully integrated R&D model. That combined R&D effort, we believe, will accelerate our ability to take the great science in our laboratories into the clinical space obviously producing new medicines for patients,” Jenkins says. “The company invests more than €1 billion a year in R&D and we are really building a strong syn-

ergy across our scientific and our clinical endeavors, which we think is critical for modern day biopharmaceutical organizations.”

The company’s innovation strategy involves a blend of internal and external R&D efforts. Partnerships developed with academia, biotech, and even large pharmaceutical companies ensure that Merck Serono has access to a broad spectrum of innovation, Jenkins says.

“We do believe that the next wave of innovation in medical research will emerge from these virtual communities, which share goals coming together to solve these medical needs. So about 50% of our pipeline consists of organic, internally advanced initiatives from our discovery organization and about 50% form external collaborations, which is an extremely important part of our R&D model,” Jenkins explains.

In addition to traditional business development channels, MS Ventures, the corporate venture arm of Merck Serono, provides seed funding for start-up companies. Merck Serono has used this funding model to give new life to promising drug candidates that otherwise may have been discarded in the 2012 restructuring. The company established a €30 million fund to provide seed financing for employees seeking to start their own research organizations. To date, eight spin-off and start-up companies have received financing. The company also seeks IPs coming out of academic institutions in specific geographic areas, including Israel and China.

Internal R&D is conducted at facilities in Boston, Darmstadt, Beijing, and Tokyo. In April 2013, the company announced an expansion of the Billerica, Mass., site. The facility, renamed the EMD

Company Stats

Company

Merck Serono, biopharmaceutical division of Merck KGaA
EMD Serono, a subsidiary of Merck KGaA (US and Canada)

Headquarters

Darmstadt, Germany
and Rockland, Mass.

Top Management

Belén Garijo, President and Chief Executive Officer

Stefan Oschmann, Head of Pharmaceuticals

Annalisa Jenkins, Head of Global Research & Development

Susan Herbert, Head of Global Business Development & Strategy

Thierry Hulot, Head of Global Manufacturing & Supply and *ad interim* Head of the Biosimilars Unit

No. of Employees

15,600 worldwide

Key Research and Product Areas

Oncology

Immunology

Neurodegenerative diseases

Fertility

Endocrinology

Cardiometabolic Care & General Medicine

Biopharmaceutical Facilities

R&D: 4

Manufacturing: 5

Analytical Testing: 2

Serono Research & Development Institute, will host early-stage drug discovery research through to clinical development. Since 2008, the company has invested more than \$90 million in the facility, which currently houses more than 380 employees. “We still have ways to go,” says Jenkins. “We will, in the next year or so, accommodate more than 600 employees here. On a global basis, one-third of Merck’s R&D talent will be based in Boston.”

Expansion of the EMD Serono Research and Development Institute in Billerica, Mass. will allow the company to strengthen its footprint in the United States.



QUALITY FOCUS FOR MANUFACTURING

The processing and manufacturing arenas have been “an interesting journey” for Merck Serono, says Jenkins, who is responsible for quality management in manufacturing on a global basis. “Today we have an end-to-end fully integrated development and manufacturing capability, which supports the continuum of our early/late phase and launch and, of course, supply in lifecycle management.”

The company has five biopharmaceutical manufacturing sites in Switzerland, Spain, Italy, as well as two analytical formulation development sites.

“We have many years of experience in modern day biologics development, scale up, and manufacturing. In the last couple of years, there has been specific focus on quality and we certainly needed to pay particular attention to how we are sustaining and building our capability in this space to be fully compliant with all the standards that we operate within on a global basis,” says Jenkins.

In December 2011—about the same time Jenkins joined the company—FDA issued a warning letter citing quality issues at three Merck Serono facilities in Switzerland and Italy. Noting that some of the cGMP violations occurred at all three facilities, FDA wrote that it “expects Merck KGaA to undertake a comprehensive and global assessment of your manufacturing operations in all your facilities to ensure global, adequate, and timely resolution of the issues, including making needed improvements to your quality system.”

“We have made very significant progress in bringing our organization really into full compliance,” Jenkins reports.

The company also is expanding its network for small molecule manufacturing and increasing internal and external capacity through partnerships with CROs for its general medicines portfolio. “This involves processing and attending to processes across our global network as well as a lot of technology transfer, which occurs between internal and external

sites, so that we can increase capacity and agility of our manufacturing network,” she says. “Like everybody, we continue to expand our presence in China which is a key growth market for Merck Serono, strengthening our manufacturing capabilities there, and that’s a natural next step process in organization.”

R&D/MANUFACTURING COLLABORATION

The collaboration between R&D and manufacturing is critical, particularly with global supply networks and regulatory requirements. At early phases in the R&D continuum, Merck Serono organizes manufacturing launch teams to prepare for seamless transfer of projects from R&D to manufacturing. These teams provide expertise in process development, scale-up, and standards that will be required, and develop the appropriate quality by design and quality management systems needed to support the drug submission.

“Of course in the early development phase, the major properties of the drug are being continually adjusted through the manufacturing process. The improvement of this process during clinical development has to be done in a very thoughtful way and be fully integrated from very early to late stage to lifecycle,” says Jenkins.

The company uses a platform approach for analytical and downstream development, and uses generic and proprietary chemically defined media for upstream and downstream processing. This process is used to speed first-in-human use and to fit into large scale for both late-phase and commercial production.

Amid concerns about drug supply shortages due to manufacturing issues, regulatory authorities

are urging R&D organizations to ensure, early in the R&D process, that the CMC module is ready to support successful regulatory filings. Ongoing support of a robust manufacturing process that meets global regulatory standards also is a top priority.

“This really is a major discussion topic at the moment, and I think internally at Merck Serono we have been paying a lot of attention to this seamless, fully integrated partnership between manufacturing and R&D.”

TRANSFORMATION FOR INNOVATION

Over the past few years, Jenkins says, “We have been very focused on making sure that we undergo this really extreme transformation of our organization, fixing some basics, looking at the external world, thinking about where we

We have been paying a lot of attention to this seamless, fully integrated partnership between manufacturing and R&D.

want to be as an organization in the next 5 to 10 years, and making sure we prepare with the right internal framework and the right people in the right culture to drive the next chapter for our organization, which is all about sustainable long-term growth.”

The company also is building collaborative long-term partnerships with stakeholders such as FDA, EMA, agencies in China and Japan and around the world, Jenkins says, “because ultimately for me, this will be the key to our mid- and long-term success as we hope to make great things hap-

pen from our pipeline and as we ask our employees to really think about living innovation as an innovation-led organization in the future.”

In October 2013, Merck Serono officially opened its new global headquarters in Darmstadt. “I can say this really is a significant and exciting step ahead for the campus in Darmstadt, which is proud of being there for 344 years. It is really now looking to reestablish a modern day, forward-looking global biopharma footprint for its biopharmaceutical business moving forward.” **BP**

A Renewed Focus on R&D, Manufacturing, and Quality

Merck Serono has spent the past few years refocusing and reprioritizing its pipeline, reinventing its R&D structure, rebuilding a quality focus for manufacturing, and fixing some basics. Annalisa Jenkins, executive vice-president, head of global research & development for Merck Serono, discusses the transformation in an interview with *BioPharm International*.