Pharma outsourcing: Challenges + opportunities

Address by

Ann Gidner,

Head of Marketing & Sales
Business Line Pharma
Saltigo GmbH

(Please check against delivery)

(2008-1502e)
Good morning, ladies and gentlemen,

The custom manufacturing market, which the world's research-oriented pharmaceutical manufacturers generate through their outsourcing activities, is a key market for Saltigo. Mr. Schmitz has already given you an introduction on this topic.

I would now like to analyze this market in a little more detail and tell you where and why we think it offers good business growth opportunities for Saltigo.

In 2006, over 40 percent of global sales of pharmaceutical products were recorded in the United States of America. Europe and Japan followed considerably behind. These three markets together accounted for more than 80 percent of world pharmaceutical sales, worth around 640 billion US dollars.

Some 90 percent of this – about 580 billion US dollars – are patented drugs, the remainder are generics. In value terms, the share of active pharmaceutical ingredient or API is only eight percent, or 52 billion US dollars. And only about one quarter of this value is produced outside the pharmaceutical companies. Nevertheless, this outsourcing market for patented active ingredients and intermediates has a global volume of some 12 billion US dollars or around 8 billion euros – the figure Mr. Schmitz has already given you. This is a very significant
market where a large number of companies operate. According to our estimates, the top twenty companies in this segment have a joint market share of around 35 percent.

The global view: Top 10 pharmaceutical companies

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Headquarters</th>
<th>Annual sales (US$ bn)</th>
<th>R&amp;D spending (US$ bn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>U.S., New York</td>
<td>44.28</td>
<td>7.440</td>
</tr>
<tr>
<td>2</td>
<td>GlaxoSmithKline</td>
<td>UK, London</td>
<td>32.96</td>
<td>5.708</td>
</tr>
<tr>
<td>3</td>
<td>Sanofi-Aventis</td>
<td>France, Paris</td>
<td>32.34</td>
<td>4.789</td>
</tr>
<tr>
<td>4</td>
<td>Novartis</td>
<td>Switzerland, Basel</td>
<td>24.96</td>
<td>4.484</td>
</tr>
<tr>
<td>5</td>
<td>AstraZeneca</td>
<td>UK, London</td>
<td>23.95</td>
<td>5.356</td>
</tr>
<tr>
<td>6</td>
<td>Johnsons &amp; Johnson</td>
<td>U.S., New Brunswick, NJ</td>
<td>22.32</td>
<td>6.312</td>
</tr>
<tr>
<td>7</td>
<td>Merck &amp; Co.</td>
<td>U.S., Whitehouse Station, NJ</td>
<td>22.01</td>
<td>3.848</td>
</tr>
<tr>
<td>8</td>
<td>Wyeth</td>
<td>U.S., Madison, NJ</td>
<td>15.32</td>
<td>1.262</td>
</tr>
<tr>
<td>9</td>
<td>Bristol-Myers Squibb</td>
<td>U.S., New York</td>
<td>15.25</td>
<td>2.746</td>
</tr>
<tr>
<td>10</td>
<td>Eli Lilly and Company</td>
<td>U.S., Indianapolis, IN</td>
<td>14.65</td>
<td>3.025</td>
</tr>
</tbody>
</table>

Total: approx. US$ 45 bn


(2008-1502e-2)

Because the United States is the world’s largest pharmaceutical market, it is not surprising that there were six U.S. companies among the top ten international pharmaceutical companies in 2005. The first German one was down in 14th place, Boehringer Ingelheim.

In 2005, the R&D expenditures of these top 10 amounted to some 45 billion US dollars, which was equivalent to around two thirds of the industry’s global research expenses.
This regional focus is very significant for us because Saltigo sees itself as a partner to these innovative companies. We take into account the fact that, in 2005, a total of some 67.5 billion US dollars was invested by the pharmaceutical segment in R&D, mainly in North America and Europe.

Our goal is to become the hub of a global network of ideas and products that springs from these R&D projects. I have used colored arrows here to denote this flow of project ideas and products. This business is affected to only a minor extent by competitive pressure from low cost suppliers from Asia.

With our solid expertise in process development and our high-tech production platform, Saltigo already plays an important role in the production of new chemical entities. This is an activity to which we have dedicated ourselves – together with innovation-oriented pharmaceutical companies from all over the world.
Ladies and gentlemen,

A decisive factor in Saltigo's success is our partnership with pharmaceutical manufacturers that enables us to be involved in new developments from the beginning of clinical trials. We feel that the innovation climate in the pharmaceutical industry is stable, and we are confident that new innovative products will move up to take the place of the many active ingredients that will lose their patent protection in the next few years.

This is also backed up, for example, by statistics from the Food and Drug Administration (FDA) on new drug applications (NDAs). Since the low in 2001, the figure has been continuously on the rise again.
To establish a direct presence in the highly attractive market of North America – and in particular on the US west coast – our US based affiliated company LANXESS Corporation a few weeks ago opened a new production site in Redmond in the US State of Washington specifically for our Pharma business line.

Already very soon, active pharmaceutical ingredients for early clinical testing up to and including Phase IIa will be produced there. For such applications, substances are initially required on a laboratory and pilot scale, with speed and flexibility being absolutely vital to provide optimal support for drug development.

The Redmond site complements our expertise in Leverkusen perfectly. Here in Leverkusen we are optimally equipped for the production of larger quantities – among other things with our new multi-purpose unit. Whenever we serve as a synthesis partner and accompany an active ingredient from initial laboratory development through registration onto the final market, it opens up significant value-adding potential for us. This is why we consider such long-term partnerships the basis for our continued success.
Here is a picture of the Redmond facility. The buildings and equipment were taken over from a competitor, which means that LANXESS Corporation will be able to begin production for us within a very short time. The building, which has a surface area of nearly 25,000 square feet, was erected in 1993 and will employ approximately 25 people. It will produce substances in a typical batch size of 2-10 kg.
In Redmond there is a development lab with ten workplaces and a GMP kilo lab, which is equipped with glass reactors and is also able to perform pressure reactions. There is also a GMP pilot plant with several glass-lined steel reactors with capacities of 200 and 400 liters, as well as apparatus for isolating the reaction products.

Depending on requirements, we will be able to expand these resources at short notice.
As you probably know, CGMP stands for "Current Good Manufacturing Practice", a regulatory system for the development, production and quality control of active pharmaceutical ingredients and intermediates.

CGMP plays a key role not only in Redmond but also in Leverkusen, especially in the new unit in Building O10. To meet the increasing need for CGMP production, we are very pleased to now present the O10 API plant, which supports both existing Saltigo Pharma projects but also offers capacity for new CGMP projects.

Particularly with active ingredient production, the specifications generally become stricter the closer one gets to the active ingredient in the production process. This is illustrated by the top diagram.

In the bottom diagram, I have endeavored to explain that CGMP is a complex set of rules. The actual GMP specifications – shown here as a grey block – form only the basis. On top of that we have the specific requirements of our customers – shown here in red. Finally, Saltigo also follows its own rules and guidelines, shown in violet. The latter are summarized in our CGMP manual and cover all our activities, including, for example, the names of the people responsible and descriptions of workflows, the building requirements and the technical specifications.
This CGMP system comprises three levels and is a core component of any customer audit or official audit. In the past, it has always been evaluated positively.

**Key success factors for Saltigo in Pharma custom manufacturing**

<table>
<thead>
<tr>
<th>Solid technology toolbox</th>
<th>Key competencies for the pharmaceutical industry:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous innovation efforts</td>
<td>Chiral compounds</td>
</tr>
<tr>
<td>Decades of experience</td>
<td>Catalyzed coupling reactions</td>
</tr>
<tr>
<td>Dedication to quality</td>
<td>Fluorine chemistry</td>
</tr>
<tr>
<td>Reliability and responsiveness</td>
<td>Challenging chemistry</td>
</tr>
<tr>
<td>Confidentiality</td>
<td></td>
</tr>
<tr>
<td>Serving you in all scales</td>
<td></td>
</tr>
</tbody>
</table>

(2008-1502e-9)

Ladies and gentlemen,

Saltigo wants to accompany its customers in the pharmaceutical industry from the original development of the active ingredient to the marketing of commercial quantities. To do this, we can count on a number of positive factors to ensure success. In the pharmaceutical business, in particular, this means:

- Having a broad technology portfolio that also takes full account of modern technologies, and
- Having experience not only in the art of synthesis but also in process development and quality management – I have already mentioned CGMP.

In all sectors, we can rely on experienced, highly qualified personnel, not least for patent and regulatory matters. The protection of our customers' intellectual property and strict confidentiality are taken for granted.

Particularly in the pharmaceutical segment, we attach major importance to four core technologies. One of them is the production and use of chiral substances that exist in the form of mirror-inverted molecules, so-called
enantiomers, of which, as a rule, only one is normally used as an active ingredient. Maintaining this optical purity can be a very complex challenge.

Another of Saltigo's core technologies is the industrial application of catalytic coupling reactions. I will come back in more detail to fluorine chemistry and challenging reactions in a minute.

Example – Process development: Automatic and parallel

Advantages

- Speed and throughput
- Safety
- Environmental protection

In process development, we want to operate even more efficiently and faster than before – also in "challenging" cases, for example when performing reactions under high pressure or using hazardous substances like chlorine or phosgene. We make use of the automated parallel reactions already established in many other segments. Whenever suitable equipment has not been commercially available, we have closed the gaps with our own developments.

Innovations developed by the custom manufacturing partner are key to the success of a project in pharma outsourcing. I would like to give you a few examples from Saltigo:
In chemical research, too, Saltigo offers its customers a certain lead through innovation.

One of our specialty fields is organofluorine chemistry. We have about 40 years of experience in this segment, and thousands of substances are immediately available. Our portfolio of synthesis procedures currently permits the production of around 22,000 fluoroorganic compounds.

Our "Fluorine Team" uses this know-how to support customers who are looking for an effective and competent research partner. During the R&D phase, we help our customers to deal with the problem that around half of all pharmaceutical and agrochemical intermediates and active ingredients nowadays contain fluorine. Our Fluorine Team offers individual services extending from consulting and contract synthesis of research quantities through R&D partnerships to the generation of complete substance libraries on behalf of the customer.
Under the term "challenging chemistry", we group reactions involving either specific hazardous substances or highly exothermic reactions. The handling of corrosive, explosive, combustible or toxic substances, or reactions in which a great deal of thermal energy is released and has to be discharged under controlled conditions, necessitate top qualifications, experience and a marked safety awareness.

We are also able to handle such reactions with absolute safety. They often offer considerable advantages, especially if there is no other economically viable method of synthesis available. Inexpensive, readily accessible starting materials can often be used with simple, well-known processes. Such syntheses require few reaction steps and provide products of high yield and purity.
An example of a hazardous substance reaction is the use of phosgene for the highly efficient build-up of oxazoline-diones, which occur, for example, in ACE inhibitors to combat high blood pressure. The alternative – DCC-induced coupling – only succeeds in moderate yields and produces byproducts that can make it necessary to perform a complicated purification of the product. Apart from that, this reaction necessitates far more solvents and reagents and produces more waste.
Typically, reactions of organometallic compounds are highly exothermic. This is true, for example, for reactions of lithium or magnesium compounds, such as the coupling shown here for producing an aromatic phosphane. Such reactions are performed at Saltigo on a scale of up to 6,300 liters. If required, the process can also be carried out under CGMP conditions.

Phosphanes are important in the previously mentioned catalyzed coupling reactions, because, as ligands, they stabilize the catalytically active transition metal centers. They are used, for example, to couple α-chiral amines without racemization – and that on a 1,000-liter scale.
Ladies and Gentlemen,

The name Saltigo stands for a combination of modern equipment and facilities, for a comprehensive technology portfolio and for many years of expertise and experience.

Our recipe for success for our customers in the pharmaceutical industry is that we not only have this expertise and adapt it continuously to the needs of the market, but above all, that we use it entirely to the benefit of our customers – from early clinical research to the commercial product.
All this makes us an ideal partner to innovative companies operating in innovative industries. And the pharmaceutical industry is a very important representative of this class.

Many thanks for your attention.

Forward-Looking Statements
This news release contains forward-looking statements based on current assumptions and forecasts made by Saltigo GmbH management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.