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CarboGen and AMCIS: Dedicated to Drug Development

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Abstract: For 44 years of combined history, CarboGen and AMCIS have benefited from their prime location in Switzerland. The combined companies have flourished in a nation that delivers geographic, legislative, and economic benefits that are particularly appealing to developing pharmaceutical companies that serve global markets. Firmly committed to their combined mission of reducing the time, cost, and risks associated with drug development, CarboGen and AMCIS routinely apply innovative science and technology for industrial advantage. Together, these leading Swiss pharmaceutical industry suppliers serve to further science and advance therapeutic treatments that improve the human condition around the world.

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Solutia's Pharmaceutical Services Division (Solutia PSD) combines the world-class chemistry skills of CarboGen (Aarau and Neuland, Switzerland) and AMCIS (Bubendorf, Switzerland) to provide seamless drug substance development and commercialization services.

Dedicated to reducing the time, cost, and risks associated with drug development, CarboGen and AMCIS focus on supporting the drug development process from bench to market. Together, the companies deliver **integrated chemistry services** that include:

- Early-stage services, such as process research and rapid supply of active pharmaceutical ingredients (APIs), through CarboGen; and
- Late-stage services, such as process development and API manufacture for clinical trials and in-market supply, through AMCIS.

As a world leader in chemistry development, CarboGen and AMCIS are committed to science, speed, and quality. In 2003 and 2004, they served more than 60 pharmaceutical firms, including seven of the ten largest companies worldwide. Currently, they generate more than 60% of their revenue from companies based in the US.

Integral to the development of many leading drugs, CarboGen and AMCIS play an important role in bringing new drugs to market. Ultimately, our work helps clients make critical decisions more efficiently and progresses drug candidates through the development pipeline, and into the hands of patients, more quickly (Fig. 1).

Swiss Origins of Innovation and Success

With broad international capabilities and unique pharmaceutical expertise, CarboGen and AMCIS each trace their roots to Switzerland. It was here that they be-

gan separately, flourished individually and eventually joined forces under ownership by Solutia Inc., St. Louis, Missouri, US.

CarboGen AG was founded in 1990 at the University of Zürich to conduct process research and develop new APIs for early clinical trials for the US-based, research-oriented pharmaceutical industry. In 1994, the company moved to a new facility in Aarau, just west of Zürich, and in February 2000, CarboGen became the early phase drug substance development unit of the Solutia Pharmaceutical Services Division. Today, CarboGen employs a staff of 200 at locations in Aarau and nearby Neuland.

AMCIS AG was founded in 1983 as a spin-off from CIS-Pharma to perform innovative contract research and development for the global life sciences industry (CIS-Pharma which was started in 1952 by Dr. Werner Schaefer, the inventor of the first synthetic penicillin in 1947, develops pharmaceutical products and technologies, which are licensed to both multinational and start-up companies). AMCIS AG success-



Fig. 1. Seamless drug development

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Fig. 2. CarboGen and AMCIS headquarters

fully promoted its contract manufacturing services and by 1996 opened a new state-of-the-art production facility. In 1997, AMCIS was recognized for the exemplary quality of this facility, when the FDA conducted their inspection that yielded no FDA 483 observations. In 2000, Solutia Inc. acquired AMCIS for its late-phase drug substance development and commercial production capabilities. Today AMCIS employs a staff of 120 at its location in Bubendorf (Fig. 2).

A Swiss Legacy of Security and Stability

Switzerland's geographic location offers numerous benefits to the pharmaceutical industry, has been instrumental in the successful development of CarboGen and AMCIS and remains a unique competitive advantage for the group. Benefits of the Swiss location include close proximity to European markets, access to suppliers and key services, diverse cultures and multiple language capabilities, with English well-established as the language of business. Paired with the fact that it offers one of the best-maintained and developed infrastructures in Europe, Switzerland provides the ideal location from which to maintain and operate CarboGen's and AMCIS's state-of-the-art development and manufacturing facilities.

CarboGen and AMCIS credit Switzerland's tradition of high productivity – the country currently ranks second among the world's leading national economies for overall productivity [1] – with their long-

standing reputation for precision and efficiency in the completion of all projects. This tradition has arisen out of low capital and labor costs, which are reinforced by a wealth of world-renowned universities, technical and R&D institutions, all ensuring the ongoing presence of a highly educated technical workforce. Since 1995, wages have remained stable, and productivity has risen. As a result, CarboGen and AMCIS can depend on competitive labor costs to manage project resources and budgets efficiently.

Among its other advantages, Switzerland is consistently ranked among the top business-friendly countries [1]. Low corporate taxes, long-term political stability, guaranteed protection of free competition and intellectual property, together with a particularly strong legal system enhance the appeal of CarboGen and AMCIS. Furthermore, Switzerland offers a long tradition of economic and financial stability, including low inflation and interest rates that is reassuring to CarboGen and AMCIS clients.

A Successful Integration of Two Cultures

CarboGen and AMCIS stand out among drug development service providers by offering an expanded and integrated platform of services that allows for seamless drug substance development. This integration enables both companies to enhance the level of service they can provide clients as they continue to evolve and grow as a united Swiss company.

The delivery of truly integrated drug development services is a challenging task that requires the full alignment of both CarboGen and AMCIS. Historically, different stages of the pharmaceutical development pipeline have been best served by particular organizational skills and cultures, which are considered critical business assets and must remain untouched. In order to allow for a seamless drug development process from bench to market, CarboGen and AMCIS revised that traditional thinking. In doing so, they managed to successfully integrate at the level of the working processes and systems – management, operations, quality, sales and project management and information technology – and also preserve the unique cultures and skill sets of each organization.

Joint management is at the basis of the integration between the two organizations, and it is supported operationally at all levels. In order to integrate CarboGen and AMCIS into one organization with superior process development capabilities, the companies have implemented several key practices that enable them to leverage downstream and upstream knowledge. These practices include job rotations, technical staff transfers and the formation of joint scientific teams. As a result, the company's collective awareness of the conditions and problems that can be encountered in commercial production allows for better anticipation in process research at the early phases of production. The resulting process technology more effectively facilitates late stage and commercial production.

Additionally, all sites are equipped with multipurpose equipment and with complimentary capabilities and technologies; thereby facilitating further the transfer of processes and the proximity of their locations fosters collaboration among staff. A common quality management system for all CarboGen and AMCIS sites ensures quality throughout both organizations.

Integration also occurs at the sales and project management level where clients have access to a blended team of one sales and one project management team member. Each team member has full responsibility and accountability for the business process and the management of the project. Communication among technical staff is also structured to ensure the efficient progress of the project.

Finally, state-of-the-art information technology systems allow CarboGen and AMCIS employees to collaborate securely and exchange key project data. Project management is supported by enterprise resource planning (ERP) systems specifically customized for early stage development at CarboGen and for production at AMCIS. A fully integrated laboratory information management system (LIMS) manages the

large volume of analytical data necessary to support the early development projects. Integration of the information technology systems is ensured by a single IT organization across all sites with common server hardware, software and application standards, common application portfolio and a common intranet platform.

New Frontiers of Pharmaceutical Technology

In 2003, recognizing a growing market need, CarboGen and AMCIS began expanding into the field of highly potent API production – a specialized technology that enables the two companies to advance the development of highly potent substances, such as oncologics. To develop this capability, the companies leveraged their internal scientific, quality assurance, and engineering expertise together with close relationships to customers and suppliers of equipment and technical concepts.

December 2004 marked the final stage in the completion of a state-of-the-art containment facility in which these highly potent substances can be handled, researched and manufactured in quantities appropriate for testing and commercial distribution. A combination of infrastructure and highly evolved processes and safety practices ensure that every aspect of this facility is completely segregated to avoid cross contamination and ensure worker safety, product quality and environmental control.

The containment facility is based on an innovative cascade of protection systems.

Within this comprehensive system, individual staff members rely on the personal protective equipment only as a final protection or back-up at the end of a complete protection cascade.

Earlier in 2004, CarboGen and AMCIS further extended this capability to the development and scale-up of anti-cancer drug conjugates. The application of this technology has the potential to greatly improve the effectiveness of cancer therapies and the quality-of-life for patients by decreasing a highly potent drug compound's toxicity to healthy cells while increasing its selectivity to better target tumor cells. As a result, once approved by the FDA, new oncology treatments may be safer for patients in higher doses, and with reduced risk of side effects.

CarboGen and AMCIS are currently supporting the development of drug conjugates on behalf of clients who are leaders in this emerging field. The projects involve process research and development as well as scale-up and production of batches of conjugated APIs for clinical trials. The hybrid nature of these compounds makes their processing, purification, and analysis highly technical. Work with them demands a multidisciplinary approach combining expertise in the fields of both small and large molecules for process R&D, scale-up and current good manufacturing practice (cGMP), and must also be supported by high-potency and highly specialized analytical capabilities.

CarboGen and AMCIS believe the highly potent API market represents an important area of future industry growth. It is esti-

imated that 25% of the 6,500 drugs currently under development contain highly potent compounds. On the polymer-drug conjugate side, more than ten new candidates have entered phase I or phase II clinical trials in the last decade. With the promising phase II results of some representatives of this class, the first expected FDA approval of the new therapeutic cancer treatment should generate significant interest and investment.

Creating a Bright Swiss Future

For 44 years of combined history, CarboGen and AMCIS have benefited from their prime location in Switzerland. The combined companies have flourished in a nation that delivers geographic, legislative, and economic benefits that are particularly appealing to developing pharmaceutical companies that serve global markets. Firmly committed to their combined mission of reducing the time, cost, and risks associated with drug development, CarboGen and AMCIS routinely apply innovative science and technology that advances the industry. Together, these leading Swiss pharmaceutical industry suppliers serve to further science and advance therapeutic treatments that improve the human condition around the world.

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