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Drug Development
& World-wide Registration

Debio R.P. S.A.
Advanced Drug Delivery Systems
Development & Manufacturing

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SWISS COMPANY DEBIO RECHERCHE PHARMACEUTIQUE ANNOUNCES AGREEMENT WITH INHALE SUBSIDIARY SHEARWATER CORPORATION TO DEVELOP NEW HYDROGEL DRUG DELIVERY TECHNOLOGY

(Martigny, Switzerland) March 12, 2002 -- Debio Recherche Pharmaceutique (Debio R.P.) based in Martigny, Switzerland, today announced an agreement with Shearwater Corporation (Huntsville, Alabama) to develop and commercialize an innovative hydrogel technology to deliver macromolecular drugs and proteins as polyethylene-glycol (PEG)-conjugates. This contract between Shearwater and Debio R.P. provides for an assignment in Debio R.P.'s name of the patents derived from research financed by Debio R.P. in exchange for royalties payable to Shearwater on sales of products containing PEG hydrogels that result from the collaboration. Shearwater has also been granted a license to make and use these PEG hydrogels outside the drug delivery field in exchange for royalties payable to Debio R.P.. The first patent resulting from collaboration work on one type of injectable PEG hydrogel was granted in the United States.

The platform technology assigned to Debio R.P. consists of a new family of hydrogels, one of which releases proteins *in situ* as PEG-conjugates. According to Dr Piero Orsolini, CEO of Debio R.P.: "This feature clearly confers significant advantages over other types of hydrogels, such as better tissue penetration, possibility for tumor targeting and an increased therapeutic index, particularly for the release of proteins with a short duration of action. The delivery of proteins used as anti-cancer drugs is of particular interest to us, since this therapeutic area is currently a strategic focus."

Proteins such as interferon, erythropoietin, and growth hormone, used as drugs for severe and chronic diseases, such as some viral diseases, cancer, severe anemia and growth deficiencies, must be administered to patients by multiple daily injections. Controlled release systems to deliver such proteins over a longer duration ensure better compliance and reduce patient discomfort. Because proteins are very fragile molecules, they need a suitable environment to maintain their integrity and fully deploy their activity. Hydrogels can provide this environment: by their structure (cross-linked hydrophilic polymers), their particular characteristics (capacity to swell rapidly in water while maintaining a three-dimensional network), their continuous delivery pattern, biocompatibility and biodegradability. Upon administration, the cross-linked polymer degrades so that the loaded protein can be released in optimum conditions.

This additional platform will complement the advanced drug delivery technologies that have been developed in-house, including Debio R.P.'s leading platform utilizing poly-lactic glycolic acid (PLGA) for peptides and hydrophilic and hydrophobic low molecular weight molecules and several PEG-conjugate platforms suitable for passive targeting of cytotoxic molecules to the tumor site.

Debiopharm, Debio R.P. and Debioclinic are an established and proven group of three synergistic and complementary companies, that has a successful track record in developing, registering and bringing to the market new chemical entities both in Europe and in the United States. Products successfully registered and launched include oxaliplatin for advanced colorectal cancer and triptorelin pamoate for prostate cancer, both market leaders in their therapeutic areas. Specialized in oncology, hormonal and niche products for serious medical conditions, Debiopharm is a partner of research institutions, pharmaceutical and biotechnology companies who seek to develop and register their drugs. Debio Recherche Pharmaceutique (Debio R.P.), Debiopharm's sister company, is a leading world player in the research, development and manufacturing of polymer-based controlled release injectable formulations for peptides and proteins, including proprietary technologies suitable for other therapeutic modalities such as soluble polymer drug conjugates for parenteral administration. Debio R.P. also carries out scale-up under current good manufacturing practice (cGMP) and has an FDA-inspected plant. Debioclinic, the third Debio company, is fully dedicated to clinical development.

Shearwater Corporation, a research-based drug delivery company, is a leader in advanced PEG technology for enhancing the delivery performance of most major drug classes, including macromolecules such as peptides and proteins, and small molecules. Shearwater is a subsidiary of Inhale Therapeutic Systems, Inc. (San Carlos, California). Inhale provides a portfolio of leading performance-enabling drug delivery technologies and expertise to help pharmaceutical and biotechnology companies maximize the performance of their compounds.

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For further information, contact:

Mrs. Kim Bill
VP Business Development & Licensing
Debiopharm S.A.
Tel.: +41 21 321 01 11
Fax: +41 21 321 01 69
kbill@debio.com

Dr Piero Orsolini
President & CEO
Debio R.P.
Tel.: +41 27 721 79 00
Fax: +41 27 721 79 01
porsolini@debiorp.ch