Drug Development
EXECUTIVE

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Ascendia Pharmaceuticals: Sophisticated Formulations for Poorly Soluble Drugs

ASCENDIA PHARMA

Many NCEs and repurposed drugs in early development are challenging to formulate in an adequately bioavailable form due to their poor solubility in water. To overcome these challenges, many formulation approaches have been developed by the drug delivery industry. Among the most successful technologies have been particle size reduction to nanometer-size drug crystals with greater surface area for dissolution, production of amorphous solid dispersions for reducing the energy required for dissolution, nanoparticle systems for dissolving/dispersing a hydrophobic drug in either a lipid or polymer material, and the use of nanoemulsions to dissolve a drug in an oil phase of an oil-in-water system. Ascendia was established to provide pharmaceutical companies with a contract research partner that can provide all of these technologies in order to efficiently determine which approach is most suitable for a given molecule. Drug Development & Delivery recently interviewed Jingjun (Jim) Huang, PhD, CEO and Founder of Ascendia, to discuss the company's unique vision and strategy.

Q: Why did you decide to establish a new company in the drug delivery field?

A: After 15 years of big pharma experience as a pharmaceutical scientist in the field of formulation development, I strongly believed there were unmet needs in drug delivery of poorly water-soluble compounds - both in discovery and in life cycle management.

More than 50% of NCEs and drug products approved by the FDA fall in the category of BCS II or IV, and delivery of these compounds in a soluble form is required for many reasons. For example, adequate solubility is needed to provide sufficient drug loading for parenteral products, to establish a sufficient concentration gradient for oral absorption through the GI tract, and for a

high influx for topical and ocular dosage forms. Many early stage compounds are abandoned due to poor biopharmaceutical properties, such as low solubility or permeability. In addition, in a race to be the first one to market, many sub-optimized formulations of poorly soluble drugs are rushed through development - this creates an opportunity to reformulate these medicines to enhance their safety and efficacy.

The main mission of Ascendia is to capture the current unmet needs in formulation science by utilizing our drug development expertise and advanced formulation technologies to provide sophisticated formulation solutions for poorly water-soluble compounds. We want to bring out "a new life" for difficult-to-formulate compounds or existing medicines that will eventually help patients prevail over their disease and enhance their quality of life.

Q: What is the company's current strategy?

A: We focus on three fast-growing market segments: 1) development of novel 505 b(2) formulations of existing medicines, especially niche hospital drugs and injectable pharmaceuticals; 2) development of ANDA dosage forms for drugs with solubility and/or stability challenges; and 3) offering contract product development services to other leading biotech and emerging pharmaceutical companies. In all of these segments, we leverage our in-house drug delivery platforms: EmulSol for nano-emulsions, NanoSol for nano-particles, and AmorSol for amorphous solid dispersions. Our technologies are suitable for oral, parenteral, and topical products, so we have a broad capability to develop novel products for ourselves and our partners.

Q: What technologies does Ascendia offer to its partners, and what makes the company unique?

A: We have a suite of nanoparticle technologies - nanoemulsions, amorphous nanodispersions, and lipid/polymer based nanoparticles - so we can assess the feasibility of a broad array of formulation options to improve a drug's bioavailability and create formulation solutions with enhanced biopharmaceutical properties suitable for clinical scale-up. We execute rapid, comprehensive, and cost-effective programs for difficult compounds, and provide both development and analytical testing services. We partner with emerging, discovery-stage pharmaceutical companies to provide early stage formulations, with generic companies that seek enabling technology, and with specialty pharmaceutical companies that need development of a product for clinical testing.

The unique feature that makes our company stand out in the crowded CRO field is our sophisticated and thorough drug development programs, in combination with our advanced nanoparticle-based formulation technologies. We ensure the successful translation of a drug program from discovery to a marketable dosage form. Our team of scientists has decades of big pharma experience in discovery pharmaceutics, formulation approaches, and clinical development. We understand the essential properties of compounds and the finished dosage forms required for successful early and late-stage development. For our discovery-stage partners, we provide a tailored formulation solution for compounds that have promising efficacy in an animal/human model, but yet have some deficiency in their biopharmaceutical properties, such as poor water solubility. Often our formulation solutions provide our partner with new intellectual property for their products.

Q: How do your nanoemulsion and nanoparticle technologies improve a drug's bioavailability?

A: Nanoemulsions have droplet sizes in the range of 50 to 500 nanometers. Ascendia produces nanoemulsions using a high-shear process called EmulSol. After a suitable oil phase is chosen, a mixture of the oil, water, and the drug substance is processed through the homogenizer, creating a suspension of the oil droplets in a water phase. As the drug substance is significantly more soluble in the oil phase than in the water phase, the vast majority of the drug is solubilized within the interior of the oil droplets. Thus, when the nanoemulsion is delivered to the body, the drug substance is more readily bioavailable. Ascendia's nanoemulsion process is novel in that it uses no organic co-solvents, and a minimal amount of

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surfactants. By minimizing surfactants and eliminating solvents, Ascendia's nanoemulsions are much more suitable for pharmaceutical applications. A nanoemulsion can be used to deliver a poorly palatable drug in liquid form for a pediatric development program, significantly reduce the irritation and injection site pain for a parenterally delivered product, or be used to develop a topical formulation with superior clarity and bioavailability properties. In addition, nanoemulsions can be dehydrated and incorporated into solid oral dosage forms. Nanoparticles produced by our NanoSol technology normally have a size range below 400 nm, and the drug contained in the particle is either in crystalline or amorphous form. Formulation of a drug in a nanoparticle form significantly increases the surface area available for dissolution - a 10 to 21-fold increase in surface area can result from reducing particle size from a micronized drug substance to a nanonized drug substance. As surface area increases, the rate of dissolution increases, and bioavailability improvements may result. If a solid dosage form is desired, the nanoparticles are stabilized by adsorption onto polymer carriers - a process conducted by fluid bed coating. Alternatively, the nanoparticles can be prepared as a suspension and administered orally or by injection. Ascendia can produce nanoparticles using a wide variety of processes - bead-milling, high-pressure homogenization, microfluidics, or solvent evaporation. We can investigate the impact of nanonization with less than a gram of drug substance. Ascendia's nano-particle technologies can enable pharmaceutical products with enhanced bioavailability, reduced food-effect, and more rapid onset-of-action.

Q: How does Ascendia work with its clients? What is the business model?

A: Business development at Ascendia is focused on our clients' needs. You will find us responsive, thorough, and easy to work with. After gaining a solid understanding of a project's requirements, we provide a client with a customized proposal.

Our goal is consistent with your goal - provide quality service, exceptional insight, timely output, and fair pricing. Currently, Ascendia operates under a hybrid model: developing proprietary products for out-licensing, and offering state-of-the-art contract research for difficult formulation development projects. Our contract research projects are designed to quickly determine the viability of a technical approach, and are conducted in stages that allow us to modify a work plan as needed. Our goal is to produce an optimal product formulation for our client by understanding the compound's properties, route of administration, and bioavailability goals. Our contract research programs are done on a fee-for-service basis, and we avoid encumbering an early stage project with intellectual property licenses; in fact, we seek to add value to our clients' projects with new patentable formulations.

Q: Does Ascendia have current partners, and what kinds of projects is the company involved with?

A: Ascendia is currently working with several partners on confidential development programs, including an emerging biotech company, a specialty pharma company, a virtual, early stage discovery company, and a mid-cap pharma company. Typically, we have three kind of projects. First, working with an NCE at the discovery stage, collaborating with our partner to provide a CMC solution to bring the compound from discovery to the clinic using one of our technologies. Second, we reformulate existing medicines for a new route of administration, or to an enhanced version, to address an unmet medical need. Such products are available for co-development and out-licensing. Third, is the application of our technology platforms for the development of a generic equivalent product. Typically, those compounds chosen for an ANDA project have either a solubility, bioavailability, or stability issue that our technologies can address.

Q: So you are developing your own products? On your website, Ascendia is positioned as a specialty pharma company.

A: Yes, we are creating "innovative" specialty pharmaceutical products; however, we do not intend to market our products ourselves, but instead seek commercialization partners. Our business model is to identify products that our technology and expertise can improve the safety or efficacy of. We then conduct preclinical development, proof-of-concept studies in animals, secure IP protection for the product, and then license out to a partner for further clinical development. One such product is ASD-002 - an injectable form of clopidogrel. This important anti-thrombotic drug is only available as an oral dosage form today due to its challenging biopharmaceutical properties. Ascendia has created a parenteral form with adequate solubility and stability to be used in an acute, emergency setting - this addresses an unmet medical need. In addition to partnering our pipeline, we are actively looking for collaboration opportunities with specialty pharma or generic companies to develop sponsored pharmaceutical products.

Q: What is your vision for the company, and what are the critical success factors?

A: WWe are striving to position our company as a world-class leader in drug delivery for poorly soluble compounds. We plan to achieve this vision by expanding our expertise in nanoparticle technologies, developing an innovative drug pipeline for out-licensing, growing our team of scientists, building up a GLP/GMP manufacturing capability, and exploring new opportunities to serve emerging markets outside of the US, such as China. ◆

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