Athena files first NDA for Zanaflex

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NEW YORK—These days a host of biopharmaceutical firms—long before their lead products are commercialized—are seeking profitability through licensing, acquisitions, and partnerships. Athena Neurosciences (S. San Francisco, CA), which is focusing on neuropharmaceuticals, is an ardent adherent of this approach, as it has in-licensed several neuropharmaceuticals in advanced stages of development and is selling its own line of generic neuropharmaceuticals through its own mail-order pharmacy. Most recently, Athena filed its first new drug application (NDA) with the Food and Drug Administration (FDA, Bethesda, MD) for Zanaflex (tizanidine hydrochloride), an in-licensed, orally active, antispastic agent for spasticity of spinal-cord origin associated with multiple sclerosis (MS) and spinal-cord injury.

Athena licensed U.S. and Canadian marketing rights to Zanaflex from Sandoz Pharma (Basel), which currently markets the product in over 25 countries, capturing over $100 million in annual sales. Athena will pay Sandoz—which will manufacture Zanaflex for Athena—a licensing fee of about $500,000 for Zanaflex, as well as royalties of about 30 percent of Zanaflex sales for 10 years. Zanaflex—a muscle relaxant that reduces the excitatory input to motor neurons within the spinal cord—is believed to control spasticity through an agonistic effect on presynaptic alpha$_2$-adrenergic receptors, resulting in a reduction of excitatory neurotransmitter release.

Zanaflex's NDA contains data from three pivotal studies involving 525 patients, with one study conducted by Sandoz and the other two conducted by Athena. Of Athena's studies, one focused on patients with spasticity secondary to MS, while the other focused on patients with spasticity secondary to spinal-cord injury. Together, the three studies show that Zanaflex reduces the spasticity of MS and spinal-cord injury, without producing muscle weakness, according to Athena.

Several biotech analysts expect the FDA to approve Zanaflex in late 1995. The product will then compete with generic products—including baclofen, diazepam, and dantroline—that make up a $30 million U.S. market. "Zanaflex may expand this market if, indeed, it doesn't produce muscle weakness, which is a problem that isn't remedied by other agents," says Linda Miller of Paine Webber (New York). For his part, Stuart Weisbrod of Merrill Lynch (New York), sees Zanaflex racking up North American sales of $5 million in 1995, with these sales reaching $35 million in 1999.

Athena is already marketing an in-licensed, brandname neuropharmaceutical, Permax (pergolide mesylate), for Parkinson's disease. Last April it licensed exclusive U.S. marketing rights to Permax for 10 years from Eli Lilly (Indianapolis, IN) for $36 million, including an $18 million licensing fee and $18 million in additional payments stretched over 18 months. Lilly—which will manufacture Permax for Athena—introduced Permax in the U.S. in 1989 and is currently marketing the product in over 10 countries. A dopamine agonist that acts at both the D_1 and D_2 dopamine receptors, Permax competes largely against generic products that in 1992 comprised a $360 million U.S. market. The product brought Athena about $8 million in sales last year, and Merrill Lynch's Weisbrod sees Permax's sales rising from $14 million this year to $25 million in 1999.

Athena is also pushing a purchased, brandname neuropharmaceutical through phase III trials. Last October Athena acquired from Upsher-Smith Laboratories (USL, Minneapolis, MN) worldwide rights to Diastat, a rectally administered formulation of diazepam that treats young adults and children with acute, repetitive epileptic seizures. Athena hasn't made public how much it paid USL for Diastat or what percentage of Diastat sales USL will receive in royalty payments. Nor has Athena found a manufacturer for Diastat. Athena is currently helping the National Institutes of Health's National Institute of Neurological Disease and Strokes (Bethesda, MD) conduct Diastat's phase III trial. According to Athena, diazepam is absorbed faster with Diastat than with suppositories or intramuscular administration. Indeed, intravenously administered diazepam is up to 90 percent effective in ending severe epileptic seizures in 2 to 10 minutes. "Diastat, though, is designed to be administered, not in a hospital setting by professionals, but in the patient's home by family members," says John Groom, Athena's president and chief executive officer.

Yet only one of Athena's in-house neuropharmaceuticals has entered clinical trials. Athena is currently conducting phase I trials in the U.S. and Canada of botulinum toxin serotype B, known as AN072, for cervical dystonia. Dystonia—a neuromuscular disorder in which muscles undergo sustanied contractions—strikes up to 200,000 people in the U.S., with cervical dystonia—which affects the neck and shoulders—the most prevalent form, striking up to 40,000 Americans. When injected locally into an affected muscle, AN072 is believed to block the release of the neurotransmitter acetylcholine, weakening the muscle and alleviating the muscle spasm for up to several months. Athena has signed up the Michigan Department of Public Health (Lansing, MI) to manufacture AN072. Allergan (Irvine, CA), however, already markets in the U.S. botulinum toxin serotype A, known as Botox, which racked up sales of $19 million in 1992 treating eyelid spasms and crossed eyes. The FDA has been reviewing Botox since March 1991 for the expanded indication of cervical dystonia.

Athena's in-house neuropharmaceutical research, though, has attracted the interest of established pharmaceutical firms. Athena has joined with Lilly in a potential eight-year, $19.3 million research collaboration to develop therapeutics for Alzheimer's disease. With Hybritech (San Diego, CA), a Lilly subsidiary, Athena has entered into a potential three-year research collaboration to develop Alzheimer's diagnostics. And with Wyeth-Ayerst Laboratories (St. Davids, PA), Athena has commenced a potential three-year, $6.5 million research collaboration to develop therapeutics and diagnostics for stroke, migraine, and head and spinal-cord trauma.

—B.J. Spalding