Rare Disease Therapeutics, Inc

Products

Rare Disease Therapeutics, Inc. (RDT) is currently developing Orphan products, acquiring Orphan products through strategic alliances, and distributing Orphan products throughout the Americas. **RDT** works closely with the FDA Office of Orphan Product Development, National Organization for Rare Disorders, the National Institutes of Health, large international pharmaceutical companies, and patient advocacy groups to identify the unmet needs of patients with rare diseases and potential products to meet these needs.

ORFADIN® (nitisinone)

Rare Disease Therapeutics, Inc. launched **Orfadin®** (nitisinone), a product licensed from Swedish Orphan International AB, in the United States for the treatment of Hereditary Tyrosinemia Type 1 as an adjunct to dietary restriction of tyrosine and phenylalanine, on April 18, 2002.

Orfadin® (nitisinone): A classic example of the kind of product Rare Disease Therapeutics, Inc. pursues is **Orfadin®** (nitisinone), or 2-(2-nitro-4-trifluoromethylbenzoyl) cyclohexane-1,3-dione, for the treatment of Hereditary Tyrosinemia Type 1/HT-1, which is an extremely rare disorder afflicting less than 500 children worldwide with less than 100 in the United States. Present at birth, acute Tyrosinemia manifests within weeks or months as the infant fails to thrive. Frequent

symptoms include hepatomegaly, edema, ascites, melena, and hemorrhagic diathesis. If untreated, the disorder is fatal in the first year of life.

** Please see full prescribing information for a complete discussion of indications and usage, contraindications, warnings, precautions, adverse reactions, and overdosage.*

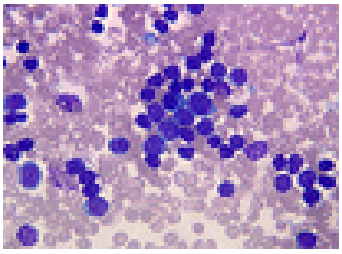
CYSTADINE® (betaine anhydrous for oral solution)

Cystadane® (betaine anhydrous for oral solution), a prescription drug product, is the first agent for the treatment of homocystinuria, a rare genetic disorder and has been demonstrated to be safe and effective for the treatment of the three primary types of homocystinuria. Cystadane® has been licensed by Rare Disease Therapeutics, Inc. from Orphan Europe effective April 13, 2007.

Cystadane® is available in plastic bottles containing 180 grams of betaine anhydrous. Each bottle is equipped with a plastic child-resistant cap and is supplied with a polystyrene measuring scoop.

** Please see full prescribing information for a complete discussion of indications and usage, contraindications, warnings, precautions, adverse reactions, and overdosage.*

Rare Disease Therapeutics, Inc. has an exciting pipeline with several potential FDA Orphan Designated products in development. Examples of these products include:



Recombinant Wolinella Succinogenes Asparaginase: The enzyme L-Asparaginase has been proven to be an effective agent in the treatment of acute lymphoblastic leukemia (ALL), however, a problem with cross reactivity (allergic reactions) may develop after several treatments limiting the use of the product.

Recent reports have established that the more intensive use of Asparaginase results in improved survival in ALL patients. Therefore, there is a need for a less-cross-reactive Asparaginase**.** Rare Disease Therapeutics, Inc. has licensed such a product in recombinant Wolinella Succinogenes Asparaginase from Children's Hospital of Los Angeles Research Institute and has the product in development through the National Cancer Institute's (NCI) Rapid Access to Intervention Development (RAID) program which was set up to provide funds and expertise for the pre-clinical development of promising drugs and biologics, and the NCI's Children's Oncology Group (COG) - a

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clinical trials cooperative group devoted exclusively to childhood and adolescent cancer research

Childhood acute lymphoblastic leukemia (also called acute lymphocytic leukemia or ALL) is a disease in which too many underdeveloped infection-fighting white blood cells, called lymphocytes, are found in a child's blood and bone marrow. In the United States, about 3,000 children each year are found to have acute lymphoblastic leukemia. Peak incidence occurs from 3 to 5 years of age. Before treatment was available, most people who had ALL died within 4 months of the diagnosis. Now, nearly 80% of children and 30 to 40% of adults with ALL are cured.

The focus of therapy for ALL is to eradicate all leukemic cells from the marrow and lymph tissue and eliminate any residual foci of disease within the CNS. Treatment is divided into three stages: (1) induction, (2) CNS prophylaxis, and (3) postremission therapy. The number of patients with ALL who enter remission, stay in remission for years, or are cured; has increased significantly over the past 30 years. However, the leukemia cells of some patients are not easily killed by drugs as those of other patients. This may lead to a failure of current treatment and/or relapse.

F (ab) $_2$ Antivenoms: Rare Disease Therapeutics, Inc**.** has entered into a joint development and distribution agreement with Instituto Bioclon, S.A. De C.V. a large , well established Mexican biotechnology company, to develop a series of much needed, high quality antivenoms for the United States and Canada.

Anascorp ®, a Centruroides immune F (ab) $_2$ is the first of a series of antivenoms in the Rare Disease Therapeutics, Inc. pipeline. Anascorp®, an F (ab) $_2$ antibody is being developed for the treatment of scorpion envenomation from the Centruroides scorpions. *Centruroides sculpturatus* is the only scorpion species with vertebrate neurotoxins whose natural range includes the United States.

It is found in southeastern California, Arizona, Nevada, southern Utah, and southwestern New Mexico. It is also found throughout the Baja California Peninsula and western Sonora, Ensenada, B.C in México. A typical "bark" or "crevice" scorpion, *C. sculpturatus* is commonly encountered under rocks, logs, the bark of trees, and other surface objects.

Centruroides scorpion envenomation produces a pattern of neurotoxicity with a spectrum of severity ranging from the trivial to life threatening. Severe envenomation, more common in small children, may involve neuromotor hyperactivity, pulmonary edema, and ventilatory compromise occasionally resulting in death. There is currently no FDA approved therapy for these envenomations

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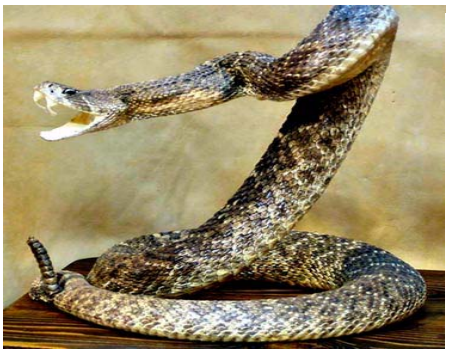
estimated to afflict up to 10,000 people annually (of which 2,000 are small children). Clinical studies are designed to demonstrate the efficacy and safety of **Anascorp** ® antivenin, *Centruroides* [Scorpion) Equine Immune F (ab) $_2$], in the treatment of systemic manifestations of scorpion sting.



Anavip® is a Crotalinae (pit viper) equine immune F (ab) $_2$ antivenom used in the treatment of envenomation by Crotaline snakes. It contains venom-specific antigen binding fragments derived from equine hyperimmune plasma. These fragments bind to venom thereby preventing or reversing the local and systemic effects of pit viper envenomation.

All vipers native to North America belong to subfamily Crotalinae, also known as the pit vipers. This subfamily includes rattlesnakes, copperheads and cottonmouths in the United States. Pit viper venoms contain a broad variety of toxins, including polypeptide "lethal factors" and "hemorrhagins" that promote capillary leak, proteases, lipases, hyaluronidase, thrombin-like enzymes that promote defibrination, and platelet –aggregating factors.

Clinical consequences of pit viper envenomation included local and systemic injury, both of which may progress for hours or days. Local injury commonly involves edema, erythema, tenderness, ecchymosis, and hemorrhagic bulla formation. Injury always begins as a small region near the fang entry site, but rapid contiguous and lymphatic spread may result in the involvement of an entire limb within a few hours of envenomation. Systemic consequences of crotaline envenomation include shock, coagulopathy, and occasionally, neurotoxicity. Crotaline snake bite still kills 5-19 patients per year in the United States.

Analatro®, *Latrodectus* immune F (ab) $_2$ antivenom is used to treat black widow spider envenomations. The genus *Latrodectus* is found worldwide with several species indigenous to the United States, including those commonly referred to as the black widow spiders.

Black widow spider venom contains several toxic components; the most significant in human envenomation is a potent neurotoxin, alpha-latrotoxin. A black widow spider envenomation can be a life threatening event especially in a young child.

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The black widow spider envenomation results in a syndrome that commonly presents with pain at the bite site but with mostly unremarkable local skin findings. However, within 30 to 60 minutes after the envenomation, the neuromuscular symptoms present as involuntary spasm and rigidity progressing proximally from the envenomation site to large muscle groups of the limbs and abdomen. Other clinical symptoms may include fasciculation, hyperactive reflexes, weakness, ptosis, priapism, vomiting, fever, salivation, perspiration, and bronchorrhea, hypertension, increased cerebrospinal fluid pressure and tachycardia early in the course changing to bradycardia late. In addition to the severe muscle pain, patients have described severe headache, anxiety and fatigue.

More information about Instituto Bioclon and the treatment of envenomation by poisonous animals can be found at **REDTOX.ORG** .

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