



## Study Supporting Herd-wide Reduction in Incidence and Severity of Diarrhea With Prophylactic Use of Neonorm Calf Published in Journal of Dairy Science

February 14, 2017

**Study Conducted in Association with Cornell University College of Veterinary Medicine and Demonstrates Significant Benefits**

**Jaguar Plans to Launch the Prophylactic Formulation of Neonorm Calf this Year in Powder Form for Administration in Liquid**

SAN FRANCISCO--(BUSINESS WIRE)--Feb. 14, 2017-- Jaguar Animal Health, Inc. (NASDAQ: JAGX) ("Jaguar"), an animal health company focused on developing and commercializing first-in-class gastrointestinal products for companion and production animals, foals, and high value horses, announced today the publication of a study titled "Prophylactic use of a standardized botanical extract for the prevention of naturally occurring diarrhea in newborn Holstein calves" in the official journal of the American Dairy Science Association, *Journal of Dairy Science*—a leading peer-reviewed general dairy research journal. The study was conducted by researchers from Cornell University College of Veterinary Medicine (Cornell). Jaguar plans to launch the prophylactic formulation of Neonorm Calf this year in powder form for administration in liquid.

Neonorm™ Calf, one of Jaguar's lead non-prescription products, has been formulated and clinically tested to help proactively retain fluid in dairy calves and reduce the severity of diarrhea—aiding the animals in avoiding debilitating, dangerous levels of dehydration associated with scours. The powder form of the product allows for ease of administration for herd-wide management.

The objectives of this study were to evaluate the prophylactic use of SB-300, the standardized botanical extract in Neonorm™ Calf, on reducing fecal water loss and diarrhea events in Holstein bull calves individually housed under a restricted whole-milk feeding regimen (6 liters/day) from 1 to 25 days of life.

A double-blinded randomized clinical trial was designed to allocate a total of 40 newborn calves into 1 of 2 treatment groups: 20 calves received (twice daily) a solution containing 500 mg of SB-300 added to whole milk for the first 15 days of life, and the other 20 calves received sterile water added to whole milk for the same period. Treatment solutions had a total volume of 10 mL per treatment. Data regarding fecal dry matter were collected to precisely measure water content in fecal samples and to define diarrhea events.

The group treated with SB-300 had significantly increased fecal dry matter during the study period compared with calves in the control group. Additionally, significantly fewer events of diarrhea were observed for calves in the group treated with SB-300 (16.9%) compared with calves in the control group (46.5%). Dehydration status was evaluated and treated accordingly; calves with moderate dehydration were offered oral electrolytes, and calves with severe dehydration were rescued with intravenous fluid therapy. Calves in the SB-300 group had fewer intravenous fluid therapies administered during the study period (1.6%) compared with the control group (3.1%). Overall fluid therapy administered (oral electrolytes plus intravenous fluids) was significantly higher for the control group (9.2%) compared with the SB-300 group (6.1%) during the study period.

"These results suggest that 500 mg of SB-300 added to the milk for 15 days can reduce the incidence of diarrhea and reduce severe dehydration in milk-fed calves," stated Dr. Andre Gustavo Teixeira of Cornell, the principal investigator of the study. "The results appear to support the potential prophylactic benefits of an easy-to-administer powder formulation of Neonorm™ Calf on reducing the incidence and severity of diarrhea and associated fluid therapy in calves."

The study results complement the results of a prior study, also conducted by Jaguar in association with Cornell, that evaluated the effect of Neonorm™ Calf on diarrhea severity and consistency in newborn Holstein bull calves experiencing diarrhea induced by enterotoxigenic *Escherichia coli* (*E. coli*). The results of this earlier study were published in *Journal of Dairy Science* in 2015.

Additionally, the positive prophylactic effect of the powder formulation of Neonorm™ in calves supports and underscores the prophylaxis data generated by the piglet studies of the powder formulation of Neonorm™ conducted in 2016 in China by Chinese investigators. As the most common disease in newborn pigs<sup>1</sup>, diarrhea has a significant impact on the global swine market as well as food security. As Jaguar announced in September 2016, the Company has signed an exclusive supply and distribution agreement for *Croton lechleri* botanical extract with Fresno, California-based Integrated Animal Nutrition and Health Inc. for dairy cattle and pigs in the Chinese marketplace.

"The standardized botanical extract in Neonorm™ Calf is sustainably derived from the Amazonian tree species, *Croton lechleri*, and has a rich history of medicinal use by indigenous peoples in the Northwestern Amazon rainforests of South America," commented Dr. Steven King, Jaguar's Executive Vice President of Sustainable Supply, Ethnobotanical Research and IP. "In recognition of this, the study recently published in *Journal of Dairy Science* acknowledges the ethnomedical expertise of the indigenous peoples of the Northwestern Amazon region who discovered how to use the latex of *Croton lechleri* for the treatment of diarrhea and other gastrointestinal conditions."

Neonatal calf diarrhea is a multifactorial disease that can be caused by infectious and noninfectious factors. In a report from the United States Department of Agriculture's 2010 National Animal Health Monitoring System study, diarrhea was the most common disorder affecting preweaned dairy heifers, with a nationwide incidence of almost 19%, and was the leading cause of death in preweaned heifers.

As announced last week, Jaguar has entered into a binding agreement of terms to merge with Napo Pharmaceuticals, Inc. ("Napo"). Napo's proprietary, patented gastrointestinal compound, crofelemer, is a first-in-class anti-secretory agent sustainably harvested from the rainforest. In October 2016, Napo launched Mytesi™, a human drug approved by the U.S. FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. Crofelemer is the active pharmaceutical ingredient (API) in Mytesi™ and also the API in Canalevia™, Jaguar's lead prescription drug product candidate for companion animals, which is being evaluated for treatment of various forms of diarrhea in dogs.

"We've now seen benefit in Neonorm™, as well as in our drug and drug product candidates at Napo and Jaguar—Mytesi™ and Canalevia™, respectively," commented Lisa Conte, president, CEO and founder of both Jaguar Animal Health and Napo. "The results of the recently completed Neonorm™ study at Cornell further highlight the common benefit, the common mechanism of action, and the common site of disease—all of which are highly conserved across all mammals."

#### **About Mytesi™**

Mytesi™ (crofelemer 125mg delayed-release tablets) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy (ART). Mytesi™ is not indicated for the treatment of infectious diarrhea. Rule out infectious etiologies of diarrhea before starting Mytesi™. If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen. In clinical studies, the most common adverse reactions occurring at a rate greater than placebo were upper respiratory tract infection (5.7%), bronchitis (3.9%), cough (3.5%), flatulence (3.1%), and increased bilirubin (3.1%). **Please see complete Prescribing Information available at [Mytesi.com](http://Mytesi.com)**

#### **About Jaguar Animal Health, Inc.**

Jaguar Animal Health, Inc. is an animal health company focused on developing and commercializing first-in-class gastrointestinal products for companion and production animals, foals, and high value horses. Canalevia™ is Jaguar's lead prescription drug product candidate, intended for the treatment of various forms of diarrhea in dogs. Equilevia™ (formerly referred to as SB-300) is Jaguar's prescription drug product candidate for the treatment of gastrointestinal ulcers in horses. Canalevia™ and Equilevia™ contain ingredients isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Neonorm™ Calf and Neonorm™ Foal are the Company's lead non-prescription products. Neonorm™ is a standardized botanical extract derived from the *Croton lechleri* tree. Canalevia™ and Neonorm™ are distinct products that act at the same last step in a physiological pathway generally present in mammals. Jaguar has nine active investigational new animal drug applications, or INADs, filed with the FDA and intends to develop species-specific formulations of Neonorm™ in six additional target species, formulations of Equilevia™ in horses, and Canalevia™ for cats and dogs.

For more information, please visit [www.jaguaranimalhealth.com](http://www.jaguaranimalhealth.com).

#### **Forward-Looking Statements**

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's plans to launch the prophylactic formulation of Neonorm Calf this year in powder form for administration in liquid, the Company's intention to develop formulations of SB-300 in horses and species-specific formulations of Neonorm™ in additional target species, and the Company's plan to develop formulations of Canalevia™ for cats and dogs. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this release are only predictions. Jaguar has based these forward-looking statements largely on its current expectations and projections about future events. These forward-looking statements speak only as of the date of this release and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond Jaguar's control. Except as required by applicable law, Jaguar does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

<sup>1</sup>Diarrhoea or Scour. Retrieved July 24, 2016, from <http://www.thepigsite.com/pighealth/article/276/diarrhoea-or-scour/>.

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