

Incitive Reports Successful Results for Lead Compound

Key points:

- Incitive's lead compound, ICV0019, reduced disease in a mouse model of inflammatory bowel disease
- Administration of ICV0019 orally and intravenously were effective

Brisbane, Australia. 26 June 2007: Incitive Ltd (ASX code: ICV) today announced positive results from its first animal model of disease using its lead compound, ICV0019, in reducing the clinical symptoms of inflammatory bowel disease (IBD).

Incitive is developing several compounds isolated from bromelain, including ICV0019, as drugs to treat a variety of diseases. Bromelain is an enzyme extract derived from pineapple stems and is regarded by the US Food and Drug Administration as safe. It has been used since the 1950s as an anti-inflammatory agent to treat swelling after trauma or surgery.

The study involved 21 mice with induced colitis (intestinal inflammation). Six control animals were compared with ICV0019-treated mice – nine were administered ICV0019 intravenously at 5, 10 and 20 mg/kg and six were administered ICV0019 orally at 5 and 50 mg/kg (n=3 animals per group). Both the oral and intravenous routes of administration of ICV0019 effectively reduced intestinal inflammation, diarrhea, loss of body weight and rectal bleeding, commonly associated with IBD.

Incitive now plans to conduct further preclinical studies to determine ICV0019's optimum dose regime, dose timing and to identify the most effective route of administration. Further animal studies are planned to determine its clinical utility in diseases such as rheumatoid arthritis and graft versus host disease - a side effect of a bone marrow or stem cell transplant that occurs when new bone marrow or stem cells (the graft) reject or attack the patient's body (the host).

Mr Donald Home, Chief Executive Officer of Incitive, commented: "While this study was only intended to provide an indication of ICV0019's ability to affect disease in this model, we were very excited to see that the ICV0019-treated groups were significantly different from the control group. Critically the results indicate that both oral and intravenous administration of ICV0019 were effective in the treatment of IBD.

"The indication that both oral and intravenous methods are effective is a successful outcome and further validates the compound's promising potential as a therapy for IBD. Once we have established the optimum dosing conditions, we will then compare the performance of ICV0019 to current drugs available on the market for treating IBD," Mr Home added.

Dr Michael McGuckin, of the Mater Medical Research Institute in Queensland, who performed the study said, "The preliminary experiment shows that ICV0019 has potential as a promising novel therapy for the treatment of IBD. IBD is a major disease problem for both Australia and the world and has a very debilitating effect on sufferers. Left untreated or poorly managed, it can lead to long term permanent damage of the gastrointestinal system and in some cases ultimately to cancer. Further studies of ICV0019 will provide validation of the drug's ability to limit intestinal inflammation."

Current treatment options for sufferers of IBD include global immunosuppressive drugs, such as corticosteroids, and anti-TNF antibody treatments, such as Enbrel, Remicade and Humira. Each of these can be ineffective in some patients and have unpleasant side-effects creating a need for new safe therapies that are more effective treatments of the disease.

“Although much is known about the crude extract, bromelain, very little is known about its individual components. Since forming and listing one year ago, Incitive have focused on developing methods of analysis, producing recombinant material, scaling up our manufacturing and developing and testing our lead candidates in animal models, all necessary requirements of drug development programs. We are pleased that we are now able to confirm that our drug candidates do indeed have the clinical potential to treat disease,” commented Mr Home.

ICV0019 is being developed at The Queensland Institute of Medical Research, the largest medical research institute in Australia. Incitive have identified and patented several enzymes from bromelain such as ICV0019 and ICV0026 that have clinical potential to treat autoimmune and inflammatory diseases such as graft versus host diseases and rheumatoid arthritis, as well as cancer.

(ends)

About Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD) is a term used to describe two disorders of the alimentary system. The disorders are ulcerative colitis (UC) and Crohn’s disease (Crohn’s) which cause damage to the bowel through a direct inflammatory process and secondary damage through infections. IBD affects approximately 1 in 500 people and it is estimated that there are over 600,000 sufferers in the US and 43,000 in Australia (30,000 with Crohn’s and 13,000 with UC). IBD often develops or is first diagnosed in patients aged between 15 and 30 years of age.

The alimentary system is composed of many regions commencing with the mouth, followed by the esophagus, stomach, small intestine, large intestine or bowel and rectum. In general the structure of the alimentary system is composed of an inner lining and a surrounding layer of muscle and connective tissue.

UC is generally seen as an inflammation of the inner lining of the large bowel, leading to weight loss, pain, diarrhoea, bloody stools and lethargy. Crohn’s can be found in any part of the alimentary system and often involves both the inner lining and the surrounding layer of muscle and connective tissue. It is common in Crohn’s for secondary bacterial infections to take place and exacerbate the disease. In extensive disease perforations of the alimentary system occur, these can become life-threatening if left untreated. Untreated or poorly managed IBD can lead to cancer.

Treatment for UC in mild to moderate disease is commonly with a range of drugs including steroids or other immunosuppressive agents. If the disease is extensive or not responding to treatment, then surgery can be used to remove the inflamed part of the bowel. In Crohn’s, the treatment for mild to moderate disease is the same as those used for UC. Active Crohn’s is commonly treated with steroids and antibiotics if a concomitant bacterial infection is present. In cases that don’t respond, treatment may include anti-TNF antibody drugs and/or surgery to remove the most severely damaged portions of the alimentary system. Side effects may include acne, abdominal pain, weight gain, depression, lowered resistance to infections and increased risk of developing certain types of cancer.

About Incitive Limited

Incitive Ltd is a publicly-listed life science company that aims to be a leader in the development of drugs that treat inflammation and auto-immune diseases. The primary target markets are tissue/organ transplantation and autoimmune disease. Incitive’s product pipeline is novel and based on over ten years of international peer-reviewed research. The lead products include

protein drugs derived from natural sources and small molecules, all aimed to treat diseases in areas of unmet clinical need.

The lead compound, ICV0019, is a protease isolated from bromelain, a crude extract from pineapple stems. ICV0019 is a MAP kinase inhibitor and is being developed at The Queensland Institute of Medical Research, the largest medical research institute in Australia. The small molecule program targets perforin, which is responsible for tissue damage during autoimmunity. The perforin technology is being developed at the Peter MacCallum Cancer Centre in Melbourne and the University of Auckland.

More information: www.incitiveltd.com

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Appendix:

Study Description

Acute colitis was induced in 21 mice using the intestinal irritant dextran sodium sulphate (DSS). This model is widely regarded to reproduce many of the clinical features of human IBD, particularly colitis.

Study Goals

The aim of the study was to determine whether oral or intravenous administration of ICV0019 could ameliorate IBD in the DSS murine model.

Design

Acute colitis was generated in mice by exposing them to 3% DSS dissolved in drinking water and administered continuously for 7 days. Control animals administered vehicle alone (n = 6) were compared with different doses of ICV0019 administered iv (5, 10 or 20 mg/kg) or orally (5 or 50 mg/kg) (n = 3 animals per group) (n=15 ICV0019-treated animals).

Clinical efficacy was determined by assessing loss of body weight, diarrhoea and rectal bleeding. Effects on colon inflammation were determined by measuring colon length and histologic grading of colitis severity.

Results

Data show that all doses of ICV0019, whether administered orally or intravenously were effective in limiting DSS-induced colitis. ICV0019 reduced the severity of colitis, particularly reduced tissue damage (Figure 1), rectal bleeding and diarrhea. ICV0019 also reduced losses

in body weight and colon length (Figure 2). At the highest oral dose of ICV0019, adverse events were observed in some animals.

Although designed as a preliminary dose-finding study, when doses for iv administration were combined for statistical analysis (ANOVA with Tukey's post-hoc test), ICV0019 showed significant efficacy in limiting the severity of clinical severity and colon inflammation in this model. Although oral administration of ICV0019 also showed efficacy in reducing disease, groups administered ICV0019 orally were not statistically analysed because of incomplete dosing and reduced numbers as a result of adverse events in some animals.

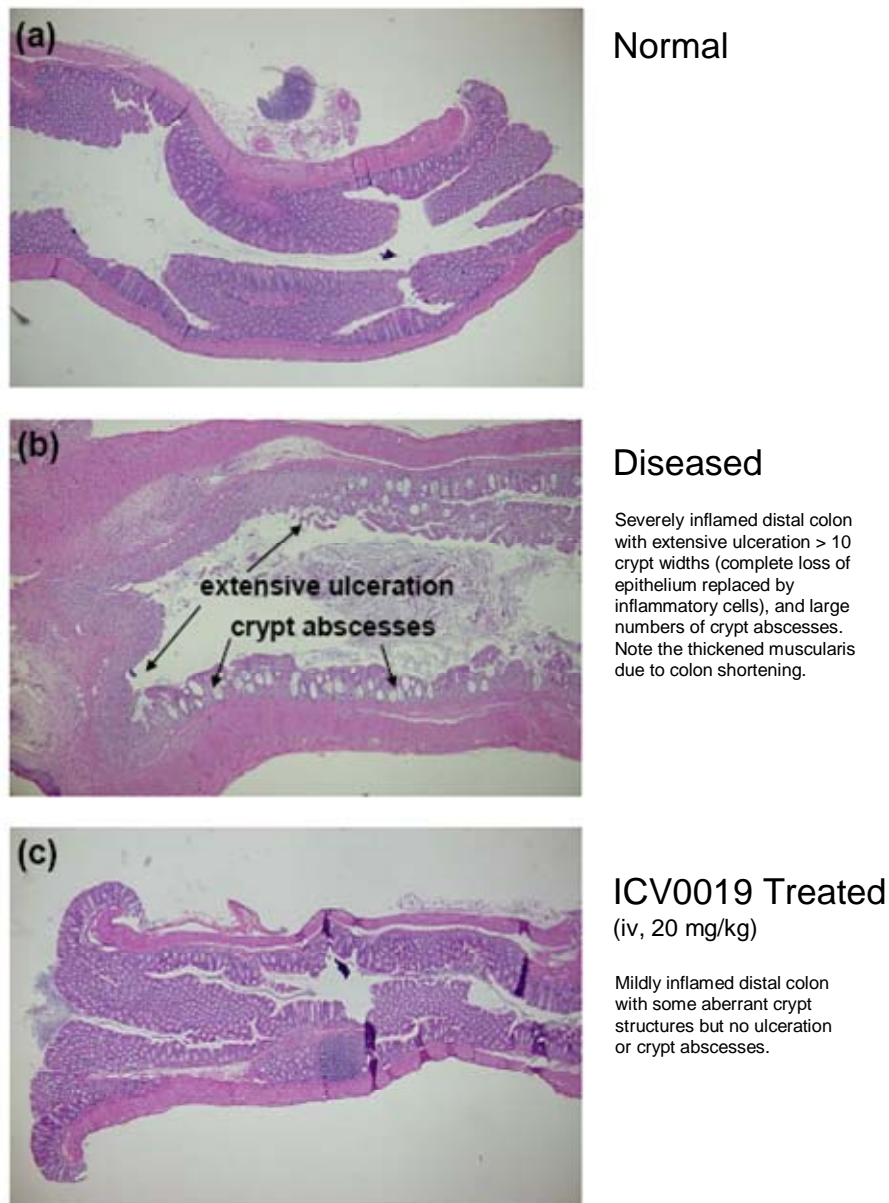


Figure 1 – Low magnification histopathology

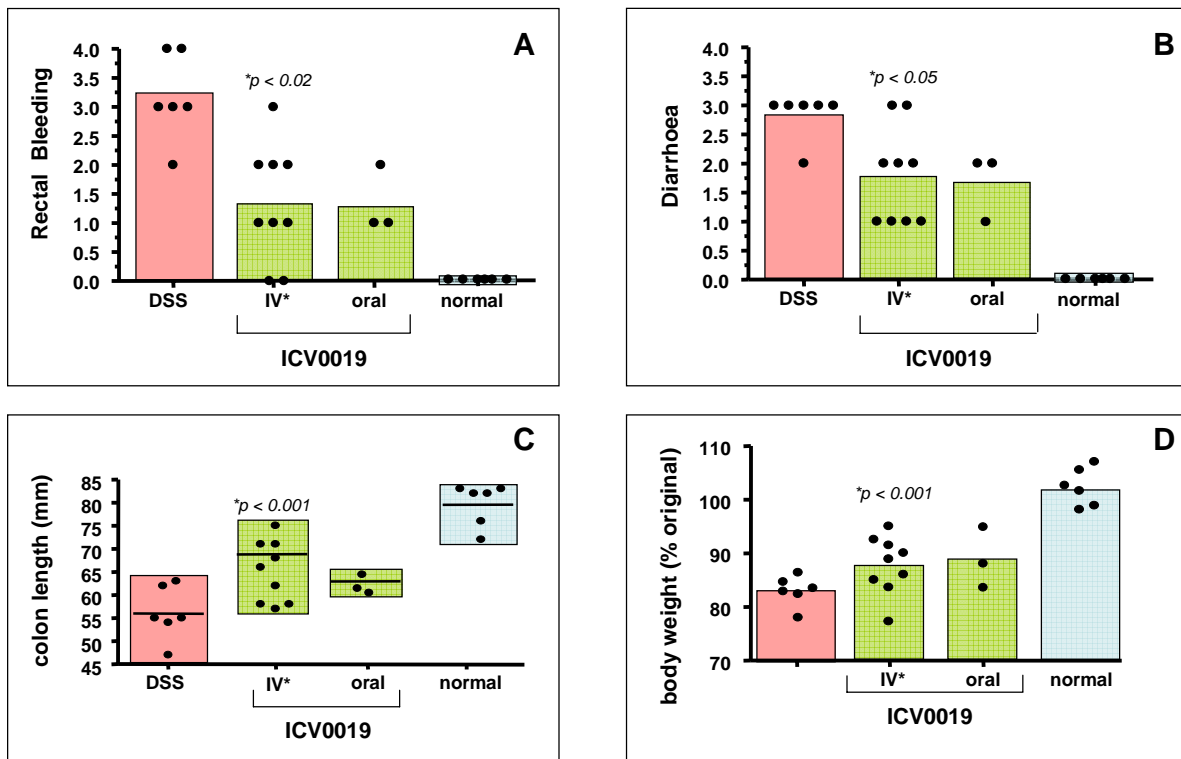


Figure 2 – ICV0019 (oral and iv) limits DSS-induced A) rectal bleeding, B) diarrhoea, C) reduction in colon length and D) reduction in body weight. Data show individual mice and columns show the mean and/or range of data.

Discussion

This study shows a clear indication that ICV0019 has potential as a novel therapy for the management of IBD.