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## **LEADING SPECIALISTS DEBATE TARGETING THE GUT-LIVER-BRAIN AXIS TO TREAT HEPATIC ENCEPHALOPATHY**

**Berlin. Tuesday 15 October, 2013, 08.30** – Leading experts from Denmark, Spain and the United Kingdom met today at a Norgine-sponsored satellite symposium at United European Gastroenterology (UEG) Week to put the case for targeting the gut-liver-brain axis when treating hepatic encephalopathy. Hepatic encephalopathy is a serious and potentially fatal disease which develops when the liver stops functioning properly. It is of particular concern as mortality rates due to liver diseases appear to be increasing or stable across Europe, in contrast to decreasing mortality rates from illnesses such as colon cancer, breast cancer and chronic obstructive pulmonary disease.<sup>i</sup>

**Professor Agustin Albillos** (Universidad de Alcalá, Spain) started the debate by exploring the concept that bacteria moving out of the gut may have an inflammatory effect which may in turn lead to brain dysfunction. He looked at animal studies which show how the immune system reacts when challenged by bacteria from a leaky gut.<sup>ii</sup> **Professor Flemming Bendtsen** (Copenhagen University Hospital, Denmark) considered whether gut decontamination might improve outcomes for patients with end-stage liver disease by looking at evidence in humans where non-absorbable antibiotics have resulted in improved outcomes.<sup>iii</sup> **Professor Rajiv Jalan** of the Royal Free Hospital/ UCL Medical School, London, United Kingdom, presented a case study reflecting his clinical experience using non-absorbable antibiotics in managing hepatic encephalopathy.

“What we know at present is that the movement of bacteria out of the gut can, in certain circumstances, lead to brain dysfunction,” commented **Professor Rajiv Jalan** who chaired the symposium. “We believe that, for many patients, brain dysfunction may be attributed to

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high ammonia levels in the gut and liver. However, there is also a substantial proportion of patients who do not fit this hypothesis and for whom we need to consider alternative pathophysiological approaches that suggest how the brain is attacked. This is particularly urgent as hepatic encephalopathy exerts a formidable burden on healthcare systems, patients and their families.<sup>iv</sup>

### **Bacterial translocation**

The human gastrointestinal tract is colonised by a dense population of micro-organisms, referred to as the bacterial flora. Although the gut provides a functional barrier between these organisms and the host, bacterial translocation is a common event in the healthy person. However, in critically-ill patients with various underlying diseases, it has been suggested that this bacterial translocation may lead to infections and consequently to a further reduction in general health. Toxins build up in the blood, then enter the brain and can present as serious neurological symptoms.<sup>v</sup>

### **About Norgine**

Norgine is a successful, independent European specialty pharmaceutical company that has been established for over 100 years and has a presence in all major European markets. In 2012, Norgine's net product sales were c€250 million and the company employs over 1,000 people.

Norgine's focus is the development and marketing of pharmaceutical products that address significant unmet clinical needs in therapeutic areas such as gastroenterology, hepatology, critical and supportive care.

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## Media Interviews

To arrange a telephone interview with Professor Rajiv Jalan, please contact Rachelle Michaels (see below).

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### References:

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<sup>i</sup> M Blachier, H Leleu, M Peck-Radosavljevic et al. The Burden of liver disease in Europe, EASL, 2013. Table 13, p46. Available online at

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<sup>ii</sup> Úbeda M, Muñoz L, Borrero MJ, Díaz D, Francés R, Monserrat J, Lario M, Lledó L, Such J, Álvarez-Mon M, Albillos A. Critical role of the liver in the induction of systemic inflammation in rats with preascitic cirrhosis. *Hepatology*. 2010 Dec;52(6):2086-95. doi: 10.1002/hep.23961

<sup>iii</sup> Vlachogiannakos J, et al. *Journal of Gastroenterology and Hepatology* 28 (2013) 450–455

<sup>iv</sup> Bass, *New England Journal of Medicine*

<sup>v</sup> Morgan M. Chapter 8: Hepatic Encephalopathy in Patients with Cirrhosis. In: Dooley JS, Lok A, Burroughs A, Heathcote J, editors. *Sherlock's Diseases of the Liver and Biliary System*. 12th ed: Blackwell Publishing Ltd; 2011

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