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## PRESS RELEASE

Zeria Pharmaceutical Co., Ltd.  
10-11 Nihonbashi-Kobunacho,  
Chuo-ku, Tokyo 103-8351

### **Announcement of the results from Phase III, double blind, placebo-controlled study of Z-338 for functional dyspepsia conducted in Japan**

Zeria Pharmaceutical announced today positive results of their Japanese Phase III study of Z-338 (acotiamide hydrochloride hydrate; “acotiamide”) for the treatment of functional dyspepsia (FD). Z-338 was developed by Zeria Pharmaceutical Co., Ltd. (Headquarters: Chuo-ku, Tokyo; President and CEO: Sachiaki Ibe; “Zeria”), and is currently being co-developed by Astellas Pharma Inc. (Headquarters: Chuo-ku, Tokyo; President and CEO: Masafumi Nogimori; “Astellas Pharma”).

The clinical trial was a multicenter, randomized, double-blind, parallel-group, placebo-controlled study to evaluate the efficacy and safety of acotiamide 100 mg three times a day for 4 weeks in patients with FD. A total of 897 FD patients from 67 medical institutions in Japan were randomized and allocated to Acotiamide group or Placebo group.

In both of two primary endpoints employed in the present study, acotiamide was statistically significantly effective when compared to placebo. Furthermore, significant improvements were observed in several secondary endpoints. The findings definitively demonstrated that acotiamide alleviated the symptoms of FD patients. No statistical difference in adverse drug reactions was noted between the Acotiamide and Placebo groups.

Based on the above results, Zeria is promptly preparing a New Drug Application for Japan jointly with Astellas Pharma. Zeria will obtain marketing authorization and manufacture acotiamide, and thereafter both companies will co-market acotiamide in Japan with a single brand name.

Acotiamide is a novel compound originated by Zeria and being developed in Europe, North America and Japan. For the development in Europe and North America, Zeria is going to select a suitable partner.

To date, no product has demonstrated efficacy or obtained marketing approval for treatment of patients with FD diagnosed by the Rome III, which is the latest version of the international classification and diagnostic criteria for functional gastrointestinal disorders. Acotiamide is expected to be the first-in-class for FD, and will be launched in Japan ahead of the rest of the world.

According to the Rome III, FD is a gastrointestinal disease comprised of subjective symptoms including postprandial fullness, early satiation and epigastric pain without any organic abnormality on gastrointestinal tract. The etiology of

FD is still unclear, but it has been shown that delayed gastric emptying is closely associated with FD.

Acetylcholine is an important neurotransmitter for gastrointestinal motility, and acotiamide inhibits peripheral acetylcholinesterase activities resulting in the improvement of delayed gastric emptying, and consequently the symptoms of FD.

Recent studies indicate that one fourth of the adult population in Japan suffers from functional dyspepsia, and FD is a disease with a high prevalence rate.

Zeria develops and markets pharmaceuticals for digestive diseases such as H<sub>2</sub> antagonist Acinon<sup>®</sup> Tablets 75mg/150mg, Promac<sup>®</sup> Granule 15%/D Tablets 75 containing zinc for gastric ulcer, Marzulene<sup>®</sup>-S Combination Granule/Combination Tablets 0.5ES/1.0ES for gastric ulcer and gastritis, Asacol<sup>®</sup> for ulcerative colitis, Visiclear<sup>®</sup> Combination Tablets for colon cleansing prior to colonoscopy and New Lecicarbon<sup>®</sup> Suppository for constipation. Furthermore, an additional indication of Z-103 (Promac<sup>®</sup>) for taste disorder, Z-360 for pancreatic cancer and Z-208 for hepatocellular carcinoma are under development.