

**ALIZYME PLC**

**INTERIM MANAGEMENT STATEMENT**

Cambridge UK, 19 November 2008: Alizyme plc ("Alizyme") (LSE: AZM) today publishes its Interim Management Statement ("IMS") for the period from 1 July 2008 to 19 November 2008. The IMS provides an update of the Group's operations for the period.

**Highlights**

**Cetilistat (obesity and diabetes)**

- Takeda Pharmaceutical Company Limited decision to commence Phase III development for obesity in Japan
- US\$3 million milestone payment received

**COLAL-PRED<sup>®</sup> (ulcerative colitis)**

- Headline results reported for EU Phase III clinical trial indicating safe treatment for acute ulcerative colitis
- Phase II clinical development in US with Prometheus Laboratories Inc progressing
- Commenced Phase I clinical development in Japan with TSD Japan Inc

**Operational**

**Cetilistat**

In September 2008, Alizyme announced that Takeda Pharmaceutical Company Limited ("Takeda"), its partner for cetilistat in Japan, had decided to commence Phase III development for obesity, following successful results from its Phase II study in which cetilistat was shown to give significant weight loss and significant improvement in glycaemic control over 6 months' treatment as well as improvement in other metabolic syndrome parameters. Alizyme received a US\$3 million milestone from Takeda. In addition, Alizyme may receive further development and sales milestones of up to US\$32 million, as well as double digit royalties on future sales in Japan. Takeda is responsible for all development and commercialisation costs in Japan. The decision by Takeda to progress cetilistat to Phase III studies is a key milestone in the development of this product and for Alizyme.

Alizyme continues discussions in relation to licensing this product for territories outside of Japan.

**COLAL-PRED<sup>®</sup>**

Alizyme has partnerships with Norgine BV ("Norgine"), Prometheus Laboratories Inc ("Prometheus") and TSD Japan Inc ("TSD") for the development and commercialisation of COLAL-PRED<sup>®</sup>.

Alizyme entered into an agreement with Norgine for the development of COLAL-PRED<sup>®</sup> in Europe and other territories in June 2008. Under that agreement, a further €40.75 million could be received from Norgine by Alizyme on the achievement of future development and sales milestones, as well as double digit royalty rates that increase with higher annual net sales levels. Norgine is responsible for all commercialisation costs. In July 2008, Alizyme reported trial results for its European Phase III study of COLAL-PRED<sup>®</sup> in the treatment of acute ulcerative colitis. COLAL-PRED<sup>®</sup> demonstrated superior safety and superior combined safety and efficacy compared to conventional oral prednisolone. A co-primary endpoint based on the Disease Activity Index of efficacy of COLAL-PRED<sup>®</sup> compared with the efficacy of conventional prednisolone was not met. However, COLAL-PRED<sup>®</sup> did show equivalent efficacy compared to conventional prednisolone after 8 weeks' dosing in the treatment of acute UC, based on patient reported symptoms. In addition, further review of the results confirm the potential of COLAL-PRED<sup>®</sup> for use in the maintenance of remission of

ulcerative colitis. The EU Marketing Authorisation Application (“MAA”), previously anticipated in Q4 2008, has been delayed and Alizyme is working with Norgine on the revised strategy for submission of the MAA.

Alizyme entered into an agreement with Prometheus for the development of COLAL-PRED<sup>®</sup> in North America in late 2007. Under that agreement a further US\$15 million could be received from Prometheus by Alizyme on achieving future development milestones as well as royalty rates which increase with higher annual net sales. Prometheus is primarily responsible for clinical development costs for the licensed territory. Phase II development in the US with Prometheus is progressing.

Alizyme entered into an agreement with TSD for the co-development of COLAL-PRED<sup>®</sup> in Japan in late 2007. Under that agreement, TSD is predominantly responsible for Phase I and Phase II clinical development costs, and all future milestones and any royalties earned in Japan would be shared equally between Alizyme and TSD. During the period, COLAL-PRED<sup>®</sup> has entered Phase I development in Japan with TSD.

Alizyme is in discussions in relation to commercialising this product in territories where it is not currently licensed to commercial partners.

#### **ATL-104**

Following the receipt of further funds from licensing deals, preparations for the next phase of clinical development of ATL-104, including manufacturing scale-up for Phase III clinical trials, will continue.

We are also in discussions with a number of parties in relation to licensing this product.

#### **Financial**

The research and development expenditure in the first half of the year reflected the activity associated with completion of two Phase III clinical studies. Alizyme’s outsourcing model means that with no ongoing clinical studies in the second half of the year, research and development expenditure is expected to be substantially lower than in the first half of the year.

The Interim Report 2008 referred to forecast cashflows which assumed receipt of income on achievement of milestones by third parties under existing licence agreements. Since then, the first of these, being a milestone payment of US\$3 million from Takeda has been received. Further milestones are potentially receivable in the future under existing licence agreements and are assumed in the forecast.

The forecast also included certain key assumptions with respect to the cash outflows of the Company, particularly with respect to the estimated timing and cost to completion of known clinical trial activity undertaken by third parties on behalf of the Company. Progress has been made with respect to reducing these costs and, while there remains some uncertainty, this has been reduced.

During the period, the Directors also implemented measures to reduce ongoing overhead costs, including reducing the number of staff from 23 to 13.

#### **Board changes**

During the period, Richard Forrest stepped down as Non-Executive Director and David Campbell stepped down as Finance Director and Company Secretary. Nick Blech has assumed responsibility for accounting and financial administration, reporting directly to the Chief Executive Officer, and was appointed as Company Secretary.

Commenting on today’s announcement, Tim McCarthy, Alizyme’s Chief Executive Officer said:

“We are advancing the development of our portfolio with strong support from our existing corporate partners and are progressing discussions in relation to the partnering and commercialisation of the remaining licence rights to the products in our portfolio. Through further success in partnering, we are aiming to continue to build multiple revenue streams for Alizyme.”

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Further information on Alizyme can be found on the Company's website: [www.alizyme.com](http://www.alizyme.com)

## **Editor's Note**

### **Alizyme plc**

Alizyme is a speciality biopharmaceutical development company, focused on the therapeutic areas of metabolic disorders, gastrointestinal disorders and cancer supportive care. It is developing cetilistat for the treatment and management of obesity and related diseases, such as type 2 diabetes, COLAL-PRED<sup>®</sup> for the treatment of ulcerative colitis and ATL-104 for the treatment of mucositis, a side effect of cancer therapy.

### **Cetilistat**

Alizyme's metabolic product, cetilistat, is being developed for the treatment of obesity and associated co-morbidities (including type 2 diabetes). It is a gastrointestinal lipase inhibitor that blocks fat digestion and absorption, leading to reduced energy intake, and thus weight loss. It is distinct from most other anti-obesity agents as it does not act on the brain to reduce appetite, but acts peripherally. The compound remains in the gastrointestinal tract with no significant absorption into the body. It can, therefore, be expected to have a superior risk-benefit profile to centrally acting drugs. Accordingly, cetilistat is not subject to the safety concerns generally associated with centrally acting drugs.

Roche's Xenical<sup>®</sup> is an approved obesity product and is also a peripherally acting lipase inhibitor. However, in clinical trials, cetilistat has been demonstrated to be significantly better tolerated than Xenical<sup>®</sup>, which has side effects that detrimentally affect patient compliance.

### **COLAL-PRED<sup>®</sup>**

COLAL-PRED<sup>®</sup> is a proprietary gastrointestinal product developed by Alizyme for the treatment of ulcerative colitis, an inflammatory disease of the colon that causes symptoms such as abdominal pain, bleeding, cramping, fatigue and diarrhoea. These conditions are characterised by episodes of acute flare of the inflammation, followed by periods of remission. In severe cases, surgery may be required to remove the diseased tissue. This market is dominated by anti-inflammatory steroids and 5-ASA products, which have safety and/or efficacy issues.

COLAL-PRED<sup>®</sup> is the combination of Alizyme's proprietary colonic drug delivery system, COLAL<sup>®</sup>, and prednisolone metasulfobenzoate sodium ("PMSBS"), an approved steroid in Europe. COLAL-PRED<sup>®</sup> has a coating that is broken down only in the colon; by locally occurring bacteria. This leads to topical delivery of PMSBS to the colon, rather than systemic delivery, making possible the effective treatment of ulcerative colitis without the usual debilitating side effects typically associated with such steroids.

### **ATL-104**

ATL-104 is being developed by Alizyme as an orally administered mouthwash for the treatment of mucositis of the mouth and gastrointestinal tract arising during cancer treatment. This provides ease and convenience of administration and enables local delivery of treatment for oral and gastrointestinal mucositis with no significant absorption into the body.

Mucositis is characterised by severe ulceration, bleeding and pain in the mouth and gastrointestinal tract, caused by damage to the cells that line these tissues by cancer chemotherapy and radiotherapy. The severity of the mucositis is influenced by the intensity of the cancer therapy and by the individual drugs used to treat particular cancer types. It can be a dose limiting side effect of cancer treatment and can require the

use of powerful pain relieving medications, parenteral nutrition (feeding via intravenous infusion) and antibiotic therapy to control associated infection and can be potentially life threatening.

**COLAL<sup>®</sup>**

COLAL<sup>®</sup> is a drug delivery technology which enables drugs to be taken orally and then be specifically released when the preparation reaches the colon. Achieving colonic release with conventional oral dosage forms has proved difficult because of the variation between individuals in transit times and conditions within the gastrointestinal tract. COLAL<sup>®</sup> overcomes this difficulty by covering small pellets containing the drug with a coating of ethylcellulose and a specific form of amylose (derived from starch). This coating prevents drug release in the stomach and small intestine. When the pellets reach the colon, the amylose in the coating is broken down by bacterial enzymes and the drug is released.

(Note: COLAL<sup>®</sup> and COLAL-PRED<sup>®</sup> are registered trademarks of Alizyme Therapeutics Limited)

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The identification of compounds for successful research, their progress through development and the obtaining of regulatory approvals or authorisations before marketing, manufacture and/or distribution of products is not certain or a formality.