Circassia Announces Positive Data Presented at 2018 American Thoracic Society Conference from Tudorza® Phase IV and Duaklir® Phase III Studies

Oxford, UK – 22 May 2018: Circassia Pharmaceuticals plc ("Circassia" or "the Company"; LSE: CIR), a specialty pharmaceutical company focused on respiratory disease, today announces the presentation of positive clinical data from the Tudorza® Pressair® phase IV ASCENT study and Duaklir® Pressair® phase III AMPLIFY study at the American Thoracic Society (ATS) 2018 International Conference currently being held in San Diego, CA.

Steve Harris, Circassia's CEO, said: *"With both the ASCENT and AMPLIFY studies meeting their primary endpoints, the positive data presented at the American Thoracic Society conference are highly supportive for Tudorza® and Duaklir®. As a result, we look forward to regulatory filings in the coming weeks seeking US approval for Duaklir® and an extension to Tudorza®'s US prescribing information to include the ASCENT data."*

ASCENT phase IV results[1]

ASCENT evaluated the long-term effect of the long-acting muscarinic antagonist (LAMA) Tudorza® (aclidinium 400µg twice-daily) on cardiovascular safety and chronic obstructive pulmonary disease (COPD) exacerbations. The study was conducted in approximately 3,600 patients with moderate to very severe COPD and cardiovascular disease and / or risk factors. ASCENT was unique in that 48% of patients enrolled had at least one documented previous cardiovascular event while 96% of patients included had at least two atherothrombotic risk factors. ASCENT met its primary endpoints, demonstrating that Tudorza® is effective at reducing exacerbations with no increase in cardiovascular events in this at-risk population. The ATS conference oral presentation included a number of outcome measures:

- Primary endpoint: Tudorza® reduced the rate of moderate to severe COPD exacerbations by 22% vs placebo ($p<0.001$) during the first year of treatment.
- Primary endpoint: the time to a first major adverse cardiovascular event was similar for Tudorza® and placebo (hazard ratio 0.89; $p=0.464$).
- Secondary endpoint: Tudorza® reduced hospitalisations due to COPD exacerbations by 35% vs placebo ($p=0.006$) in the first year of treatment.

Cardiovascular disease is the most common and significant comorbidity of COPD, with approximately 30% of COPD patients dying from cardiovascular conditions. Submission of a supplemental New Drug Application (sNDA) for Tudorza® is anticipated in the coming weeks to request inclusion of the ASCENT data in the treatment's US prescribing information. If successful Tudorza® will be the only LAMA marketed in the United States with COPD exacerbation reduction data and data demonstrating safety in patients with cardiovascular disease / risk factors in its label.

AMPLIFY phase III results[2,3]

AMPLIFY evaluated the efficacy of Duaklir® (aclidinium 400µg / formoterol 12µg twice-daily) compared with the product's individual components. The study, which was conducted in more than 1,500 COPD patients over 24 weeks, met its co-primary efficacy endpoints. The ATS conference presentation included both co-primary endpoints and data from a sub-study of 24-hour bronchodilation that compared twice-daily Duaklir® with the once-daily LAMA, tiotropium (Spiriva® Handihaler®):

- Primary endpoint: Duaklir® significantly increased forced expiratory volume in one second (FEV1) from baseline one hour post dose compared with aclidinium monotherapy (253 mL vs 169 mL, $p<0.0001$).
- Primary endpoint: Duaklir® significantly increased FEV1 from baseline prior to morning dose (trough) compared with formoterol monotherapy (80 mL vs 25 mL, $p<0.001$).
- Sub-study: Duaklir® significantly improved night-time and 24-hour bronchodilation (area under the curve FEV1) compared with Spiriva® (150 mL vs 60 mL, $p<0.001$ and 167 mL vs 109 mL, $p<0.05$ respectively).

Submission of a New Drug Application (NDA) seeking marketing approval for Duaklir® in the United States is anticipated in the coming weeks. The NDA will include data from the AMPLIFY study, results from two previous Duaklir® phase III studies, ACLIFORM and AUGMENT, and exacerbation data from the ASCENT trial.

About Tudorza® and Duaklir®
In April 2017, Circassia and AstraZeneca established a collaboration for the commercialisation of Tudorza® and Duaklir® in the United States. Under the companies' agreement, Circassia has responsibility for marketing Tudorza®, and AstraZeneca is responsible for completing the product's clinical studies and regulatory filings. Circassia also has exclusive US commercialisation rights to Duaklir®, and AstraZeneca is responsible for conducting the product's development and regulatory filing.

About Pressair®
Pressair® is an easy-to-use, multi-dose, breath-activated inhaler with a unique patient feedback mechanism that is approved in the US for delivering Tudorza® (aclidinium bromide) and is being used for the development of Duaklir® in the United States. Outside the US the Pressair® inhaler is marketed as Genuair®.

About Circassia
Circassia is a world-class specialty pharmaceutical business focused on respiratory disease. Circassia sells its novel, market-leading NIOX® asthma management products directly to specialists in the United States, United Kingdom and Germany, and in a wide range of other countries through its network of partners. In 2017, the Company established a commercial collaboration with AstraZeneca in the United States in which it promotes the chronic obstructive pulmonary disease (COPD) treatment Tudorza®, and has the commercial rights to pre-NDA COPD product Duaklir®. For more information please visit www.circassia.com.

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Forward-looking statements
This press release contains certain projections and other forward-looking statements with respect to the financial condition, results of operations, businesses and prospects of Circassia. The use of terms such as "may", "will", "should", "expect", "anticipate", "project", "estimate", "intend", "continue", "target" or "believe" and similar expressions (or the negatives thereof) are generally intended to identify forward-looking statements. These statements are based on current expectations and involve risk and uncertainty because they relate to events and depend upon circumstances that may or may not occur in the future. There are a number of factors that could cause actual results or developments to differ materially from those expressed or implied by these forward-looking statements. Any of the assumptions underlying these forward-looking statements could prove inaccurate or incorrect and therefore any results contemplated in the forward-looking statements may not actually be achieved. Nothing contained in this press release should be construed as a profit forecast or profit estimate. Investors or other recipients are cautioned not to place undue reliance on any forward-looking statements contained herein. Circassia undertakes no obligation to update or revise (publicly or otherwise) any forward-looking statement, whether as a result of new information, future events or other circumstances.

[1]Wise R et al. Effects of aclidinium bromide on major adverse cardiovascular events and COPD exacerbations in patients with COPD and cardiovascular risk factors. Late breaker Abstract (A7711) accepted for oral presentation (some p-values updated for oral presentation).
[2]Sethi S et al. AMPLIFY: a randomised, phase III study evaluating the efficacy and safety of aclidinium/formoterol versus monotherapy in patients with COPD. Abstract A4241/615
[3]Kerwin E et al. Effect of twice-daily aclidinium/formoterol versus monotherapy or tiotropium on 24-hour bronchodilation and symptom control in patients with COPD: results from AMPLIFY. Abstract A4235/609.
Aclidinium is marketed under a number of brand names around the world, including Tudorza®, Eklira® and Bretaris®