UCB announces new results from phase 2b open-label extension study evaluating the long-term effects of epratuzumab in SLE

- Relative to the 12-week, double-blind EMBLEM™ study, primary outcome data from the open-label extension identified no new safety or tolerability signals¹
- Relative to EMBLEM™ baseline, secondary outcome data from the open-label extension indicated that the efficacy of epratuzumab, as measured by reduction in disease activity, was maintained for over two years²
- Relative to EMBLEM™ baseline, secondary outcome data indicated that treatment over two years with epratuzumab was associated with decreases in corticosteroid use in patients receiving >7.5 mg/day¹
- Epratuzumab is an investigational medicine in clinical development and is not approved for the treatment of systemic lupus erythematosus (SLE)³

Slough (UK), June 13th 2013 – UCB today announced new data from an open-label extension (SL0008) of the EMBLEM™ phase 2b study evaluating the long-term effects of epratuzumab treatment in adult patients with moderate-to-severe systemic lupus erythematosus (SLE). The primary outcome of the open-label extension was to assess the safety of epratuzumab in patients with SLE.⁴

Relative to the 12-week, double-blind, placebo-controlled EMBLEM™ study, data from the open-label, long-term extension identified no new safety or tolerability signals.¹ In addition, relative to EMBLEM™ baseline values, secondary outcome data indicated that the efficacy of epratuzumab as measured by reduction in disease activity was maintained over two years.² Secondary outcome data also indicated that relative to EMBLEM™ baseline values treatment over two years with epratuzumab was associated with decreases in corticosteroid use in patients receiving >7.5 mg/day.¹ These data were presented this week at the European League Against Rheumatism 2013 Congress in Madrid, Spain.

Epratuzumab, licensed from Immunomedics Inc. (NASDAQ: IMMU) is an investigational medicine and the first CD-22/B-Cell receptor (BCR) targeted monoclonal antibody to be evaluated in clinical studies for the treatment of SLE. Also known as lupus, SLE is a complex, systemic autoimmune disease that affects many different organ systems, including the skin, joints, lungs, kidneys and blood.³⁵

“In EMBLEM™, a dose-ranging, phase 2b study, reduction in disease activity was observed in patients treated with epratuzumab,” said Professor Daniel J Wallace MD, Clinical Professor of Medicine, Cedars-Sinai Medical Center, California, US. “This double-blind study had a relatively short 12-week, placebo-controlled, treatment period and it was
important to accumulate long-term data on epratuzumab in the treatment of SLE. The phase 2b extension study adds new two year open-label data on epratuzumab to that already available from the 12-week, randomized, controlled study.”

EMBLEM™ was designed to identify a suitable dosing regimen for epratuzumab. A total of 227 patients with moderate-to-severe SLE received either: placebo, epratuzumab cumulative dose of 200 mg (100 mg every other week), 800 mg (400 mg every other week), 2400 mg (600 mg weekly), 2400 mg (1200 mg every other week) or 3600 mg (1800 mg every other week). In the open-label extension 203 patients from any arm of the EMBLEM™ study received 1200 mg epratuzumab at weeks 0 and 2 of 12-week cycles.

Data on epratuzumab presented at EULAR 2013

**Evaluation of the safety profile of long-term epratuzumab treatment in patients with moderate-to-severe SLE**

Safety variables were primary outcome measures in SL0008 and included duration of exposure, adverse events, infusion reactions and infections.

Exposure to epratuzumab was a median 845 days over a median 10 treatment cycles. Adverse events (AEs) caused discontinuation in 29 (14.3%) patients. The most common serious AEs were SLE flare (3.4%), lupus nephritis (2%) and symptomatic cholelithiasis (1.5%). The most common infections/infestations were urinary tract infection (24.6%) and upper respiratory tract infection (23.2%). There were no opportunistic infections and no patterns of specific serious or severe infections.

**Evaluation of long-term efficacy of epratuzumab as measured by reduction in disease activity in patients with moderate-to-severe SLE**

Secondary outcome measures in SL0008 included efficacy as measured by reduction in disease activity, and assessed by: British Isles Lupus Assessment Group (BILAG) improvement, SLE disease activity index (SLEDAI) score, Physician Global Assessment (PGA) score and combined treatment response defined as BILAG improvement without worsening, no SLEDAI worsening and no PGA worsening, relative to EMBLEM™ baseline.

The median BILAG total score was 25.0 at EMBLEM™ baseline and 9.0 at week 108. The score was 14.0 at SL0008 screening. Median SLEDAI score was 12.0 at EMBLEM™ baseline and 4.0 at week 108. The score was 10.0 at SL0008 screening. The median PGA score was 50.0 at EMBLEM™ baseline and 17.5 at week 108 with a score of 31.0 at SL0008 screening.

The proportion of patients achieving the combined treatment response was 32.5% at SL0008 screening (n=203) and 60.3% at week 108 (n=116).

**Effect of corticosteroid use of long-term epratuzumab treatment in patients with moderate-to-severe SLE**

Corticosteroid doses were monitored throughout SL0008 and was a secondary outcome measure.
Median corticosteroid dose at EMBLEM™ baseline and SL0008 screening was 10.0 mg/day. At week 116, this was 5 mg/day (n=112). Data indicated that treatment over two years with epratuzumab was associated with decreases in corticosteroid use in patients receiving >7.5 mg/day with a corresponding increase in the proportion of patients receiving lower doses or no longer receiving corticosteroids.

The proportion of patients requiring 7.5-20 mg/day and >20 mg/day decreased (49.8% and 10.8% at baseline and 33.9% and 8.0% respectively, at week 116) and the proportion of patients receiving >0–7.5mg/day or no longer receiving corticosteroids increased (33.5% and 5.9% at baseline and 45.5% and 12.5% respectively, at week 116).

**Assessment of immunological parameters to long-term epratuzumab treatment**

Secondary outcome measures in SL0008 also assessed the long-term effect of epratuzumab treatment on B-cells and other immunological parameters.

Median absolute B-cell count decreased by 50% at week 112, compared to EMBLEM™ baseline. CD22 expression on B-cells remained low relative to EMBLEM™ baseline throughout SL0008. No consistent trends were seen in median T cell counts, which remained similar to EMBLEM™ baseline at week 112 and no consistent trends were observed for IgG or IgA which remained within normal levels. IgM levels decreased slightly (-0.21 g/L by week 112). At week 48, there was little correlation between BILAG improvement rate and B-cell levels. The moderate reduction in B-cell counts and the lack of correlation supports B-cell modulation rather than depletion as a mode of action for epratuzumab.

Results presented above from the long-term extension of EMBLEM™ should be viewed in the context of an open-label study without placebo control. Further studies are warranted to confirm these findings.

**Notes to editors**

**About epratuzumab**

Epratuzumab, licensed from Immunomedics Inc., is an investigational medicine in clinical development for the treatment of SLE. Epratuzumab is the first monoclonal antibody that targets CD22, a B-cell specific protein which regulates B-cell activity through the BCR. Epratuzumab is not approved for the treatment of SLE by any regulatory authority worldwide.

**About SLE**

SLE or lupus, is a complex, systemic, autoimmune disease that affects many different organ systems, including the skin, joints, lungs, kidneys and blood. Disease activity and rate of progression of organ system damage is highly variable. SLE affects from 20 to 70 people per 100,000 population, and is rare in childhood. It is 10 times more common in women than men.
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References

About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8 500 people in about 40 countries, the company generated revenue of EUR 3.4 billion in 2012. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statements
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