2.2 | 2016 KEY EVENTS[1]

There have been a number of key events that have affected or will affect UCB financially:

IMPORTANT AGREEMENTS/INITIATIVES

- **UCB divested its nitrate business** to selected parties: In January 2016, UCB divested three cardiovascular products from its established brand portfolio to Merus Labs International Inc. (Canada). The transaction relates to nitrate products sold in Europe and selected markets and amounted to € 92 million. In May 2016, UCB handed over its nitrate franchise in China to Chinese company Jilin Yinglian Biopharmaceutical and its financial partner PAG Asia. The transaction amounted to € 60 million. In July 2016, UCB divested the remaining nitrates business in Russia and Ukraine.
- UCB entered into an agreement with Avara Pharmaceuticals Services to divest UCB's **Shannon manufacturing site** in Ireland in February 2016.
- **UCB reduces its indebtedness**:
  In March 2016, UCB exercised its option to redeem the € 300 million perpetual subordinated bonds. The perpetual subordinated bonds were issued in 2011 at 99.499% and offered investors a coupon of 7.75% per annum during the first five years.
  In December 2016, the € 500 million institutional bond matured and was repaid. The senior unsecured bonds were issued in December 2009 at 99.635%, carrying a coupon of 5.75% p.a.
- In July 2016, UCB out-licensed **UCB6352** to Syndax Pharmaceuticals to develop the antibody which is expected to be tested in clinical trials in oncology.
- The Delaware District Court confirmed the **validity of U.S. patent RE38,551** related to Vimpat® (*lacosamide*), UCB's anti-epileptic drug, in August 2016. The District Court decision is currently under appeal before the Court of Appeals for the Federal Circuit (CAFC).
- In November 2016, UCB divested ***venlafaxine ER***, for the treatment of depressive and anxiety disorders and marketed in the U.S., to Osmotica Pharmaceuticals Corp. (Marietta, GA) amounting to € 102 million.

REGULATORY UPDATE AND PIPELINE PROGRESS

NEUROLOGY

- **Briviact®** (*brivaracetam*) as adjunctive therapy for partial-onset seizures in patients from 16 years of age was approved in EU in January and in the U.S. in February 2016 and received Drug Enforcement Administration (DEA) scheduling in May 2016. Briviact® is now available to patients with epilepsy in the EU and in North America. In January, 2017, UCB filed a supplemental New Drug Application to the U.S. authorities for Briviact® as monotherapy in the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy.
- In July 2016, the Japanese regulatory authorities approved **Vimpat®** (*lacosamide*) as adjunctive therapy in the treatment of partial-onset seizures in adult patients with epilepsy. In August, Vimpat® was filed in Japan for the treatment of partial onset seizures as monotherapy.
  In August, Vimpat® was filed in the EU for partial onset seizures (POS) add-on and monotherapy in children (older than four years).
  In December, the European Commission approved a license extension for Vimpat® for use as monotherapy in the treatment of partial-onset seizures in adolescent (16-18 years) and adult patients with epilepsy, following the filing in January 2016.
- In February 2016, the Japanese regulatory authorities approved **E Keppra®** (*levetiracetam*) as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures (PGTCS).
- The Phase 2a study with **UCB0942** – aimed at highly drug resistant epilepsy patients, who failed four anti-epileptic drugs and have at least four seizures/week – showed positive top line results and will progress into further development.

All other clinical development programs are continuing as planned.

IMMUNOLOGY

- In March 2016, UCB announced top-line results from EXXELERATE, the first head-to-head superiority study of two treatments in the anti-TNF class, comparing **Cimzia®** *(certolizumab pegol)* plus methotrexate (MTX) to Humira® (*adalimumab*) plus MTX in adult patients with moderate to severe rheumatoid arthritis who are inadequate responders to MTX. The primary endpoints for superiority were not met, as results between Cimzia® and Humira® were numerically comparable. This study was designed as a treatment strategy trial in line with core principles of the treat-to-target guidelines, which advocate evaluating response early and ensuring a change in therapy for patients not responding at three months.
  In August, the U.S. Food and Drug Administration (FDA) has accepted UCB's filing for a proposed new indication for Cimzia® to treat juvenile idiopathic arthritis (JIA). Also in August, UCB reported positive topline results for RAPID-C, a Phase 3 study evaluating Cimzia® in rheumatoid arthritis in China. In September, the AutoClicks® prefilled pen was approved for the European Union as a new administration option for patients treated with Cimzia®.

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[1] From 1 January 2016 up to the publication date of this report.

In October and December 2016, UCB and its partner Dermira announced positive topline results from CIMPASI-2 and CIMPASI-1, two Phase 3, multi-center, placebo-controlled clinical trials evaluating the efficacy and safety of Cimzia® in adult patients with moderate-to-severe chronic plaque psoriasis. These studies were completed in January 2017, with the announcement of positive topline results from CIMPACT, a Phase 3, multi-center, placebo-controlled and active-controlled clinical trial evaluating the efficacy and safety of Cimzia®. The submissions of marketing authorization applications based on these three Phase 3 studies to regulatory authorities are expected in the third quarter of 2017. UCB continues to advance the science and expand the availability of data bringing valuable information to women with autoimmune diseases who are planning to build a family. This includes two Phase 4 studies, CRADLE and CRIB, which recently completed and provided positive results. During the fourth quarter of 2016, UCB presented at various scientific congresses the positive results from a multicenter study evaluating the concentration of Cimzia® in mature breast milk of lactating mothers (CRADLE). In January 2017, the second study, a multicenter study evaluating the transfer of Cimzia® from the mother to the infant *via* the placenta (CRIB), provided positive topline results. These results are planned for presentation at an upcoming scientific meeting. These results strengthen previous data on women treated with Cimzia® during pregnancy and the effect on their newborn infants, and will be submitted to regulatory authorities in Q2 2017.

> In March 2016, **UCB7665** started a Phase 2, proof-of-concept (POC) study, in idiopathic thrombocytopenic purpura (ITP); topline results are expected in Q3 2017.

> In May 2016, ***seletalisib*** started a Phase 1b study in activated PI3 kinase delta syndrome (APDS), a rare cause of immunodeficiency. The Phase 2a study in patients with primary Sjogren's syndrome (pSS) is ongoing with first results expected at the end of 2017.

> In June 2016, a Phase 1 study successfully completed with **UCB4144**/VR942, an immunomodulatory inhaled biologic for patients with uncontrolled asthma in development partnership with Vectura. The generated data package supports the continued development of UCB4144/VR942 and progression to Phase 2 which is expected in 2017.

> In June 2016, the Phase 2b program started for ***dapirolizumab pegol***, an anti-CD40L pegylated Fab being developed in systemic lupus erythematosus jointly with Biogen. The dose-ranging study aims to enroll around 160 patients for 12 months. First results are expected in H2 2018.

> In June, positive results from a Phase 1b study in patients with psoriatic arthritis (PsA) were presented at EULAR (Annual European Congress of Rheumatology) for ***bimekizumab***, an investigational humanized IgG1 monoclonal antibody rationally designed to potently and selectively neutralize the biological function of both IL-17A and IL-17F, two closely related proinflammatory cytokines. Both IL-17A and IL-17F are key drivers of chronic inflammation in many severe skin and joint diseases.
UCB started the Phase 2b program for *bimekizumab* in various indications: in psoriasis (August 2016 – with first results expected in Q3 2017), in psoriatic arthritis and in ankylosing spondylitis (October 2016 – both with first results expected in Q3 2018).

> In July, **UCB7858** for potential treatment of auto-inflammatory diseases entered Phase 1.

All other clinical development programs are continuing as planned.

BONE

> In February, UCB and Amgen announced positive top-line results from a Phase 3 study evaluating **Evenity™** (*romosozumab*) for the treatment of osteoporosis in postmenopausal women at increased risk of fracture (FRAME), which met the co-primary endpoints of reducing the incidence of new vertebral fracture through months 12 and 24.

> UCB and Amgen announced in March positive top-line results from a Phase 3 study evaluating Evenity™ in men with osteoporosis (BRIDGE), which met the primary endpoint of increasing bone mineral density at the lumbar spine at 12 months.

> In July, UCB and Amgen submitted the biologics license application (BLA) for Evenity™ to the U.S. authorities, which was accepted for review in September. The New Drug Submission (NDS) for Evenity™ was also submitted to Health Canada during the second half of 2016.

> In December, UCB and Amgen submitted an application seeking marketing approval of Evenity™ for the treatment of osteoporosis for patients at high risk of fracture for review to the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan. Evenity™ is developed in collaboration with Amgen globally, as well as with Astellas in Japan.

The **current liabilities** amounted to € 2 418 million, down € 643 million, due to decrease of income tax payables related to the sale of Kremers Urban in 2015, and the repayment of short term borrowings and bonds.

The **net debt** decreased by € 83 million from € 921 million as of end December 2015 to € 838 million as per end December 2016, and mainly relates to the underlying net profitability, the sale of non-core assets and the repayment of the Lannett note offset by the dividend payment on the 2015 results, the repayment of the bonds, payment of taxes related to the sale of Kremers Urban in 2015. The net debt to recurring EBITDA ratio for 2016 reached 0.8 after 1.12 for 2015 and thus surpassed UCB mid-term target of 1:1 two years ahead of time.

2.13 | CASH FLOW STATEMENT

The evolution of cash flow generated by bio-pharmaceuticals activities is affected by the following:

> **Cash flow from operating activities** amounted to € 427 million, of which € 726 million from continuing operations, compared to € 204 million in 2015. The underlying net profitability and the improvement of working capital is offset by the taxes paid related to the sale of Kremers Urban.

> **Cash flow from investing activities** showed an inflow of € 317 million in 2016, of which € 133 million from continuing operations, compared to € 19 million in 2015. The divestment of non-core assets from the established brand portfolio (mainly nitrates and *venlafaxine ER*) generated € 273 million and Lannett reimbursed the US$ 200 million outstanding senior unsecured loan notes, offset by the investment in tangible and intangible assets.

> **Cash flow from financing activities** has an outflow of € 1 267 million, which includes the dividend paid to UCB shareholders and the shareholders of the perpetual subordinated bond (€ 231 million), the reimbursement of the perpetual subordinated bond (€ 300 million) and the senior unsecured bond (€ 500 million), the acquisition of treasury shares (€ 49 million) and the repayment of short term borrowings (€ 107 million).

2.14 | OUTLOOK 2017

For 2017, UCB expects the continued growth of its core products driving company growth. UCB will also advance its development pipeline to offer potential new solutions for patients.

2017 **revenue** reporting is impacted by the product divestitures in 2016 as well as IFRS 15, and is expected to reach approximately € 4.25–4.35 billion. **Recurring EBITDA** should increase to approximately € 1.15–1.2 billion. **Core earnings per share** are therefore expected in the range of € 3.70–4.00 based on an average of 188 million shares outstanding.

The figures for the outlook 2017 as mentioned above are calculated on the same basis as the actual figures for 2016 as mentioned earlier in this management report as well as in the consolidated financial statements as at 31 December 2016 and 2015 with the exception of the following:

> The assumptions taken for the outlook 2017 conservatively take into account the expected restrained effect on revenue from the implementation of IFRS 15;

> Lower net sales of established brands due to divestitures during 2016 (nitrates, *venlafaxine ER*).