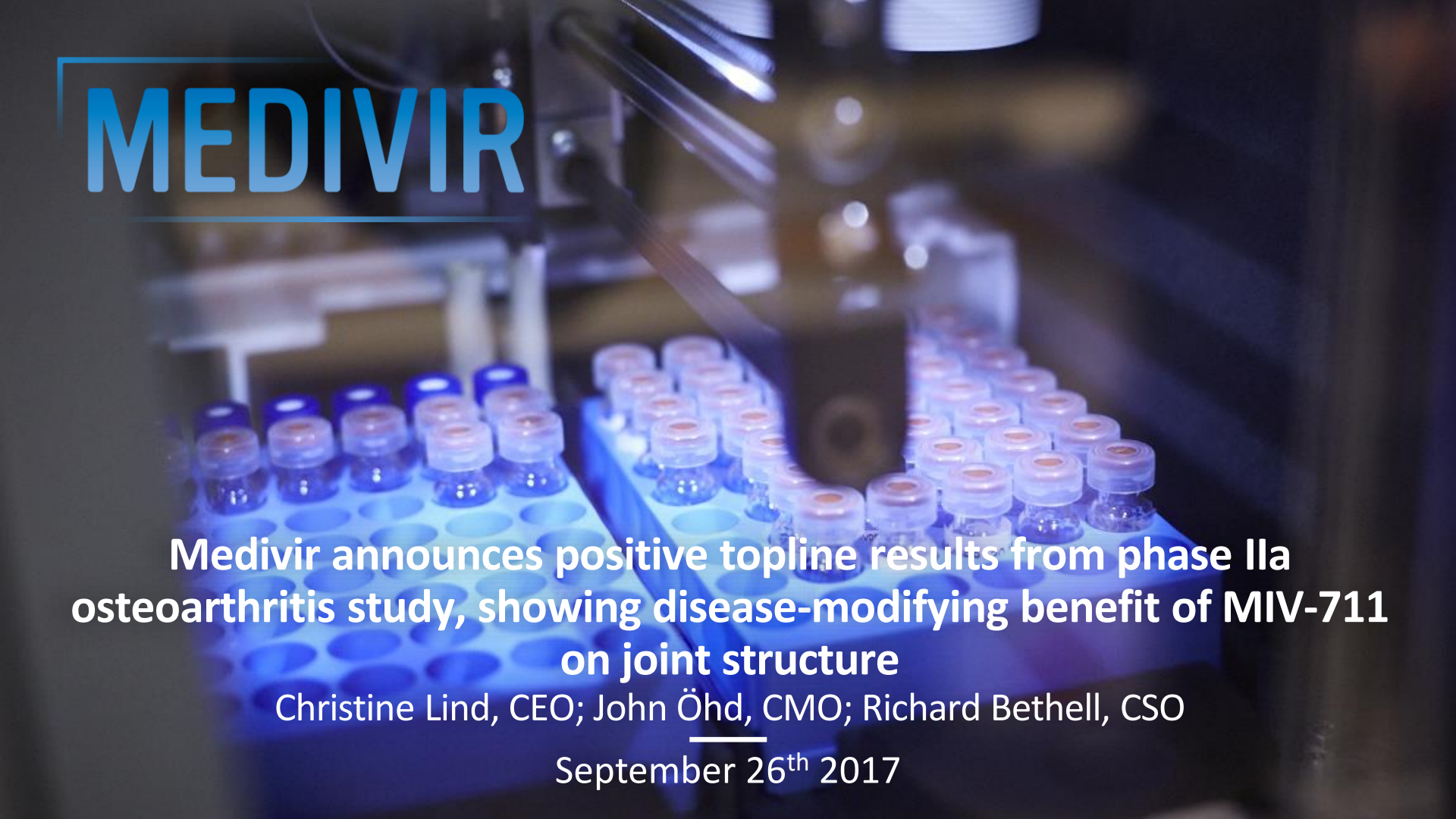


Medivir announces positive topline results from phase IIa osteoarthritis study, showing disease-modifying benefit of MIV-711 on joint structure

Christine Lind, CEO; John Öhd, CMO; Richard Bethell, CSO

September 26th 2017

Osteoarthritis: the urgent need for disease-modifying drugs

Osteoarthritis affects over 30 million adults in the US, and as many as 240 million people worldwide

- The disease is characterized by cartilage thinning and remodelling of the bone in the joint over many years
- As the cartilage is lost, and the bones in the joint change shape, the pain associated with the disease increases

There are currently no disease-modifying therapies approved for the treatment of the disease

- All approved osteoarthritis treatments affect only day-to-day symptoms
- They have no effect on the degenerative changes in the diseased joint
- There is an urgent need for Disease-modifying Osteoarthritis Drugs (DMOADs)

In order to exert a disease-modifying effect, a prospective DMOAD needs to show efficacy on the degenerative changes seen in bone and cartilage, as well as on clinical benefit

MIV-711: potential for first disease-modifying drug in osteoarthritis

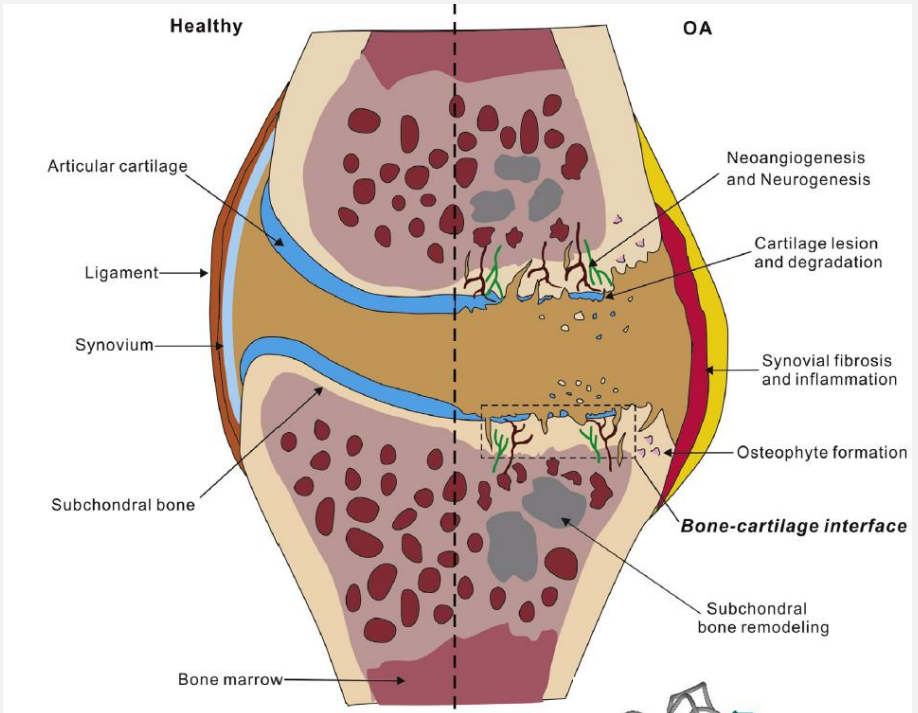
Potential disease-modifying convenient osteoarthritis drug

- Only cathepsin K (a protease) inhibitor in development for osteoarthritis
- Once daily oral administration

Preclinical and phase I data show consistent effect on relevant biomarkers of disease

- Cathepsin K breaks down collagen in bone and cartilage

Blockbuster potential with expected patent life to ~2034, including extensions



Yuan *et al.* Osteoarthritis and Cartilage (2014), 22, 1077

No disease-modifying osteoarthritis drug exists today

- Prevalence increasing due to aging population and obesity epidemic
- Current treatments are insufficient focusing on symptom relief only

Blockbuster revenue opportunity for a disease-modifying OA drug (DMOAD)

Sources: Hunter et al, Nat Rev Rheumatol, 2014; Reginster et al, Ann Rheum Dis 2013

1) >2M adults in US with moderate osteoarthritis in weight bearing joints at annual treatment cost for a drug that impacts disease progression of 3,000 USD/Year (Losina et al 2014)

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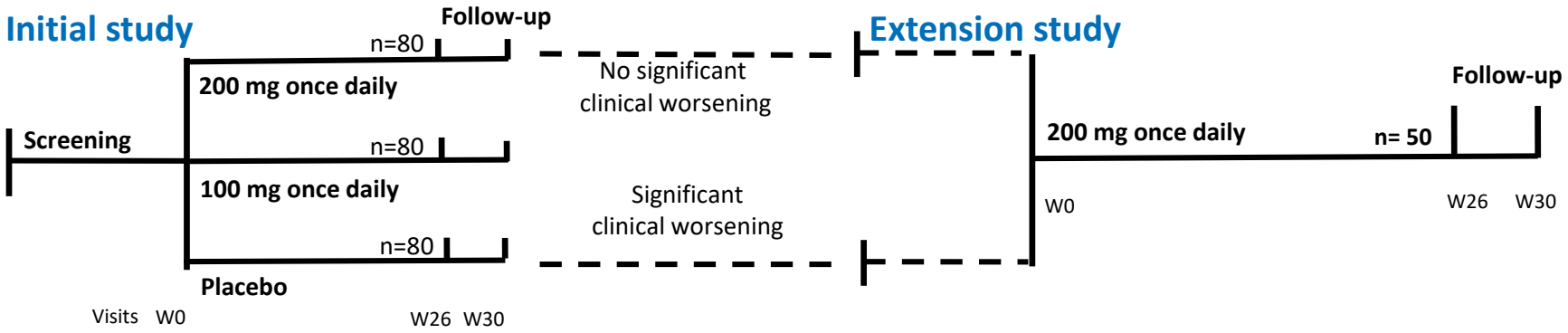
MIV-711 Phase IIa programme



- https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-003230-26/GB#A
- Enrollment completed (n=244) end October 2016
- Safety: All four DMC meetings concluded “continue as planned”

- Enrollment completed (n=50) end May 2017
- **Additional 12 and 6 month efficacy data expected 1Q’18**
- Safety: Both DMC meetings concluded “continue as planned”

Topline data from the initial study reported today

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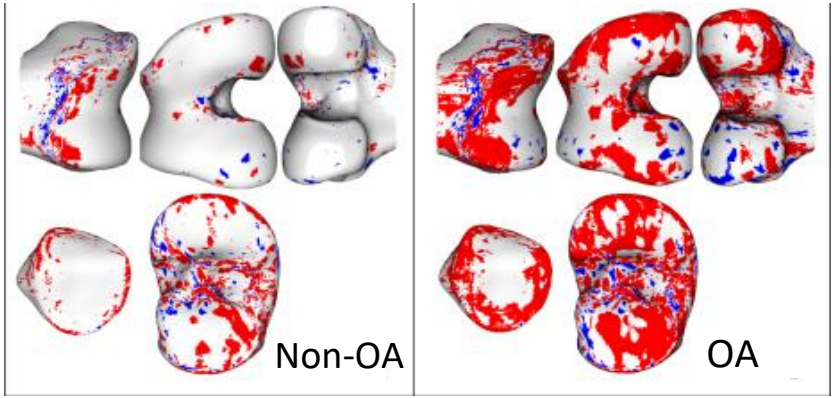
The Initial Study: MIV-711-201

MIV-711-201:

- 6 month randomized, double-blind, placebo-controlled Phase IIa clinical trial
- Enrolled 244 patients with moderate knee osteoarthritis

The principal objective was to investigate the effect of MIV-711 on joint structure degeneration

- Change in joint bone area, assessed using magnetic resonance imaging (MRI), was the key secondary endpoint
- Sensitive and precise measure of the long-term degenerative changes in joints affected by OA
- We also used MRI to investigate another key disease-relevant structural endpoint, cartilage thinning



Changes in femoral bone area over time
Picture modified from: Bowes MA, et al. Ann Rheum Dis 2015;74:519–525

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The Initial Study: MIV-711-201

Although our principal objective was to examine the effect of MIV-711 on joint structure, the primary endpoint was the change in patient-reported average knee pain

- OA pain has been shown to worsen in line with joint structure over many years
- MIV-711 is not an analgesic, and was therefore not expected to have any short-term effect on pain
- Our hypothesis is that a drug that slows or stops joint degeneration will have a long-term positive effect on pain by slowing disease progression
- It was therefore essential to understand the effect of a DMOAD on pain and other clinical symptoms in order to design future studies looking at both joint structure degeneration and clinical benefit
- In the absence of any information on what effect a potential DMOAD would have on either joint structure or pain, the trial design was powered to show an effect on pain equivalent to an analgesic

Outcomes from MIV-711-201: Joint Structure

MIV-711 demonstrated benefit on joint structure

- Patients receiving once-daily MIV-711 100mg and 200mg experienced approximately 65% reductions in joint bone area progression in the 6-month period compared to those receiving placebo (unadjusted p-values for both doses < 0.005)
- Similar to previous epidemiological cohort studies, patients who received placebo in this study showed a 1% increase in medial femur joint bone area over the 6-month treatment period
- MIV-711 also showed a benefit on cartilage degradation, with the 100mg group experiencing a 70% reduction in median loss of femur cartilage thickness relative to placebo group, and the 200mg group even showing a small increase in median cartilage thickness

MIV-711-201: Effect on Pain and other Patient Reported Outcomes

MIV-711 did not show a statistically significant effect on patient-reported numerical rating scale (NRS) pain

- A tendency was observed favouring both the 100mg and 200mg groups for patient-reported pain
- This tendency was observed consistently across other patient-reported symptoms such as:
  - Daily reporting of pain in E-diaries
  - Measures of pain associated with the daily activities
  - Satisfaction with the function of the diseased knee
- The findings on pain and other clinical symptoms from this study will enable the design of future, longer, studies aimed at demonstrating the effects of MIV-711 on both joint structure degeneration and pain and other clinical symptoms

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MIV-711-201: Safety

The study data indicate that both MIV-711 doses showed acceptable safety and tolerability for this patient population

- Six independent DMC meetings held during the Phase IIa program have reviewed unblinded safety data
- All six reviews concluded “continue as planned”

Next Steps

Medivir is seeking a partner for MIV-711

- Medivir remains focused on the development of its portfolio of oncology projects
- Larger and longer studies, and a global development and regulatory reach, will be required to maximize the value of MIV-711
- Greenhill & Co. have been appointed as advisors for the partnership discussions

Medivir will submit an abstract on the MIV-711-201 data to future scientific meeting

- Further information from MIV-711-201 will be released at the time of the first presentation of clinical data to the scientific community

Additional 12 and 6 month efficacy data from MIV-711-202 expected 1Q'18

Conclusions

- **MIV-711 has demonstrated unprecedented disease-modifying activity in osteoarthritis**
- **Although not statistically significant, consistent tendencies favouring MIV-711 were observed on pain and other clinical symptoms that will enable future studies**
- **MIV-711 has an acceptable safety profile**
- **Medivir is now seeking a partner for MIV-711**

"The finding that MIV-711 slows the degenerative changes on both bone and cartilage in knees affected by OA is an enormously exciting finding"
Professor Philip Conaghan, Professor of Musculoskeletal Medicine at the University of Leeds, UK, and lead investigator on the MIV-711-201 study

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