Press meeting

Follow up on notification from FDA regarding DeNovo application

March 1st , 2021

Emil Billbäck, CEO
Håkan Johansson, CFO

FDA Request for additional data and clarifications

The fundamental challenge, known to the Bonesupport team since the very beginning, is the lack of market standard and lack of endorsed therapeutic standard in the US for treatment of bone infections.

The entire definition of DeNovo and Breakthrough Device, is that there is “no predicate available” and “better therapeutic value than existing alternatives”. <u>This is the challenge for a pioneer regardless of market segment.</u>

The strong efficacy studies on CERAMENT G and V are done in Europe in comparison to well defined hospital/ clinic historic standard of care or literature reference:

- McNally[1], Fergusson[2] Nuffield Oxford, 100 resp 163 patients with chronic osteomyelitis: 4% infection recurrence rate versus 10%[3] with $CaSO_4$ and 15%[4] with PMMA beads
- Jahangir[5], Manchester, 51 patients with class III open fracture: 0% infection, 1.9% amputation rate versus literature of up to 52% infection and up to 16% amputation rate

The CERTIFY[6] study, 135 patients with tibia fracture, is a true RCT with specified controls, but this study is on CERAMENT BVF

1. McNally et al . Single-stage treatment of chronic osteomyelitis with a gentamicin-loaded calcium sulfate/hydroxyapatite biocomposite: a prospective series of 100 cases’ Bone Joint J 2016;98-B:1289–96 2. Ferguson, (2019). Radiographic and Histological Analysis of a Synthetic Bone Graft Substitute Eluting Gentamicin in the Treatment of Chronic Osteomyelitis. Journal of Bone and Joint Infection. 4. 76-84. 10.7150/jbji.31592. . 3. Ferguson J The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: a series of 195 cases. Bone Joint J. 2014 Jun;96-B(6):829-36. 4. Henry SL, Hood GA, Seligson D. Long-term implantation of gentamicin-polymethylmethacrylate antibiotic beads. Clin Orthop Relat Res. 1993 Oct 47-53. PMID: 8403670. 5. Jahangir et al, The usage of adjuvant local antibiotic hydroxyapatite bio-composite in the management of open Gustilo Anderson type IIIB fractures, Journal of Orthopaedics 16 (2019) 278–282 6. Hofmann Autologous Iliac Bone Graft Compared with Biphasic Hydroxyapatite and Calcium Sulfate Cement for the treatment of Bone Defects in Tibial Plateau Fractures, J Bone Joint Surg Am, 2019;00:1-15

Were not the need for clinical controls known to the Bonesupport team ?

Clinical controls were a know prerequisite for the DeNovo application. It was also highlighted by FDA during the process that selection of controls will be a challenge. Efforts were invested in 2020 to extract data and develop documentation (somewhat slowed down by the pandemic) to find comparable patient data consistently treated with another treatment modality

What happens if the additional data gathered is not meeting FDAs needs ?

A DeNovo classification and approval would make the product and indication (bone infection) combination a class II device. Failure to achieve this categorization and approval means that the product and indication combination remain in the PMA category.

The FORTIFY study, 2017-2021, is the foundation for the PMA application planned for end of 2021

Could you just not make a clinical study with a defined control ?

The challenge is the lack of standard. Different surgeons treat bone infections in different ways. To get enough patient material such study would need to be ran with major bone infection clinics (i.e. Nuffield, Oxford) at the university hospitals – the risk is that they would refuse to even do such a study with a “defined control” proven to have higher infection recurrence rate and amputation risk.

A study the size and magnitude similar to FORTIFY would overcome the challenge, however this is not our plan at this moment

What is the way forward, to meet the FDA request?

Data mining. We will work with partner clinics to extract, select, process and analyze data on patients that allows us to build a greater base of patient controls

What is the details behind the communicated time line?

As there is no existing standard when it comes to treating bone infections, different surgeons having adapted different techniques and methods. In order to increase the amount of patient control data, patient treatment data (comparable to the CERAMENT group) in respect to patient age, size of injury, comorbidities, treatment method,….will be selected. Such data work is, by experience, a bit more tedious to extract during an ongoing pandemic.

What is the chance of success for a DeNovo application on bone infection ?

We believe that there is strong historical data available in the clinician and faculty community on treatment of bone infections. This data is scattered and need processing. Our confidence in the strength of the efficacy and safety data on CERAMENT G is absolute. Our ambition is to combine these to meet the demands of FDA. This is our ambition, but we do not give guidance on probability

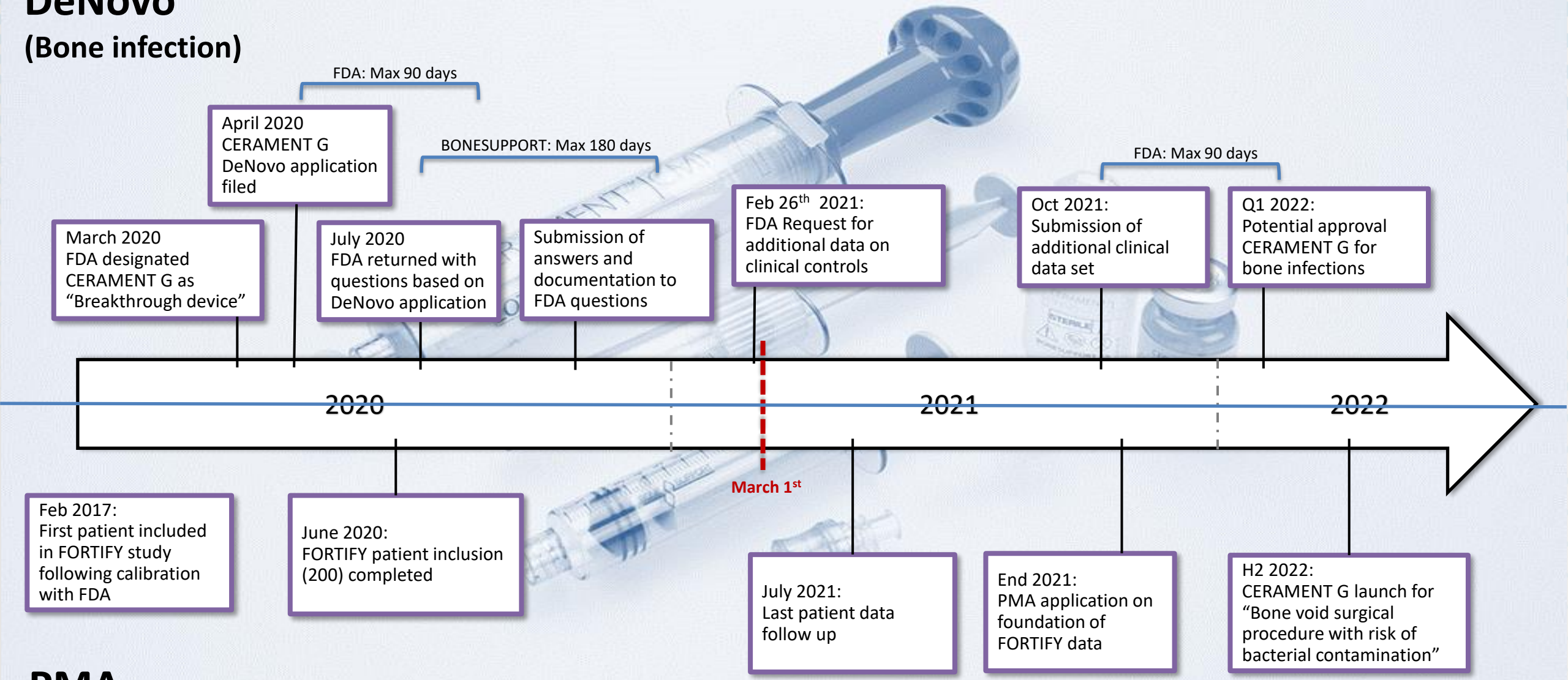
Does this change BONESUPPORT's financial position / trigger need for new share issue?

No, it does not.

CERAMENT G pathway to US market

DeNovo

(Bone infection)



PMA

(Broader set of indications, incl trauma)

Updated: 1/3 - 2021