PHARMA EQUITY GROUP

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Company Announcement No. 11

Pharma Equity Group's subsidiary, Reponex Pharmaceuticals A/S, reports highly positive final results from the phase-2 clinical trial of the company's patented drug candidate RNX-051.

Reponex Pharmaceuticals A/S (Reponex) today announced positive final results from the phase-2 clinical proof-of-concept trial of the drug candidate RNX-051, the MEFO trial, based on received high level summary from the Company's clinical site.

Reponex's MEFO-trial
This concerns the treatment of patients with right-sided colon cancer and right-sided colon polyps/adenomas (precursors of cancer) with the Company's drug candidate RNX-051. The company's clinical collaborators who have performed the trial report the following:

Background
Patients with precursor lesions to cancer in the colon (adenomas) harbor a different gut microbiota than healthy controls. Distinct bacteria have been found to influence the bowel lining by promoting chronic inflammation and through interaction with molecular mechanisms in the bowel cells that may lead to bowel cancer. A central mechanism of the bacteria with cancer promoting abilities is to produce a biofilm lining the inner surface of the bowel wall.

In patients where the cancer has already developed, it is known that distinct bacteria such as *Fusobacterium nucleatum* and *Bacteroides fragilis* shift the immune system within the tumor leading to a greater risk of metastatic spread of the cancer. The mechanisms are complex but mediated through reducing the function of immune cells that are actively killing cancer cells.

Rationale
Administering the two antibiotics fosfomycin and metronidazole (constituents of RNX-051) with distinct properties ensuring an effect both on the colon lining and inside the cancer through local administration may change the milieu leading to a reduced risk of adenoma generation and improved sensitivity to immune cells or therapies that modulate the immune system, such as immune check-point inhibitors. The MEFO trial consisted of two arms: the first in patients with adenomas (the "adenoma arm") and second in patients with cancers in the right side of the bowel (the "cancer arm"). A major aim was to change the biofilm in the "adenoma arm" and improve the tumor-related bacterial composition in the "cancer arm". In both arms there was a focus on the modulation of the immune cells in a positive way to increase their ability to kill precursor or cancer cells.

Protocol
Twelve patients and ten patients were treated in the respective arms of the trials with RNX-051 given in a muco-adhesive spray and the adenomas or tumor were removed approximately one week after the intervention. Through advanced microscopy analyses targeting certain bacteria and certain cells of

the tumor microenvironment, and advanced immune analyses including genomic analyses of both the bacteria and the precursor and cancer lesions, an in-depth overall picture of the precursor lesions and the cancer before and after treatment was obtained.

Results

In the adenoma arm, the main goal of the study, to demonstrate an impact on the bacterial biomass, was reached, with a massive reduction in the biofilm of the bowel lining (more than 30-fold reduction) one week after the treatment, from a mean of 0.003% to 0.0001% of bacterial biomass (p=0.025). An impact on the occurrence of specific immune-cells known to be crucial in the immune response against cancer was shown (macrophages and T-cells). For macrophages, the density was 2.2% in non-treated adenomas and 3.4% in treated adenomas (p=0.030), and for CD3 T-cells, the density was 524 cells/mm^2 in non-treated adenomas and 727 cells/mm^2 in treated adenomas (p=0.018). In the metagenome sequencing to assess the diversity of bacteria and the specific composition of bacteria before and after treatment, there was no reduction in the diversity of bacteria, while there was an increase of the genus *Bacteroides* (median 6.9% vs 10.8% , p=0.016), a commensal gut bacterium containing both anti- and pro-inflammatory species.

In the cancer arm, for patients with a high content of bacterial biofilm, there was a statistically significant reduction of biofilm in the tumor periphery from a mean of 0.255% to 0.013% of bacterial biomass (p=0.025). At the same time, a shift in the balance of immune cells in the tumor core could be seen, resulting in an increase in the ratio of T-cells that are particularly active in promoting tumor cell death, from a mean 0.30 CD8/CD3 ratio to a mean ratio of 1.19 (p=0.016). In the metagenome sequencing to assess the diversity of bacteria and the specific composition of bacteria before and after treatment, a clear and statistically significant effect was seen. The RNX-051 application drastically reduced or eliminated the cancer-promoting *Fusobacterium nucleatum* (median 15.2% to 0%, p=0.008) and increased the cancer-protecting Lactobacillales (median 0.23% to 2.72% p=0.023) in the tumor center without reducing the diversity of the mucosa-associated gut microbiota.

Conclusions

Based on the findings of the MEFO trial, there seems to be a clear path for establishing whether the treatment with RNX-051 as a single and even repeated dose in patients with adenomas in the bowel will lead to adenoma prevention.

For patients with colon cancer, it seems relevant to investigate whether the shift in the composition of immune cells (increase) and cancer-promoting bacteria (reduction) can result in positive effects in a larger cohort of patients and whether combination trials with RNX-051 plus immune therapy may also provide benefits for the patients with bowel cancer.

Reponex management concludes that its patented medicinal product RNX-051 appears to be highly effective for its intended purpose. Just a single local application drastically reduces tumor-associated biofilm and can even totally eliminate the cancer-promoting *Fusobacterium nucleatum* in the tumor at one week after the treatment.

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On the Company's website www.pharmaequitygroup.com further information and all published announcements can be found.

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About Pharma Equity Group A/S

Pharma Equity Group, a listed company on the Nasdaq Copenhagen stock exchange, is fully dedicated to advancing the medical projects of its subsidiary, Reponex Pharmaceuticals A/S. With an unwavering focus on healthcare, Pharma Equity Group's primary objective is to bring significant value to Reponex Pharmaceuticals' medical projects.

The company is committed to providing extensive support, resources, and expertise to drive the development and success of these projects. As a strategic partner, Pharma Equity Group works closely with Reponex Pharmaceuticals, prioritizing the advancement of innovative medical solutions and breakthrough therapies. Every effort is currently directed towards ensuring the utmost success and impact of Reponex Pharmaceuticals' medical projects, with an unwavering dedication to improving global healthcare outcomes. Only when the full potential of Reponex Pharmaceuticals has been unfolded is the intention to explore opportunities to invest in other companies. This approach ensures a strong commitment to the current medical projects and their development, while – on the longer term – remaining open to new strategic investments for continuous growth.