BACKGROUND ***(500 words)***

Background information and need for solution/product

OA is the **most common degenerative joint condition** and the **leading cause of disability worldwide**[i] [ii]. In 2017, it affected over 40 million Europeans[iii] and 303 million people globally[iv].

"Sharp, burning, predominant, omnipresent, daily activities, less confident, feel old, no foreseeable end"[v] **T**his is how patients describe OA pain**.**

The prevalence of OA is rising sharply due to an ageing population and rising obesity rates. Characterized by chronic joint pain and functional disability, **OA imposes a huge burden on patients and healthcare systems** (costs per patient per year: ca. €15k [vi] [vii] [viii]). The cost of OA in the US is estimated at $200bn annually[ix] with OA being the 3rd most common hospital admission/discharge diagnosis, ahead of cardiovascular diseases[x]. This financial burden primarily stems from over 900,000 hospitalizations, mainly for joint replacement surgery. OA increases the risk of cardiovascular mortality by 50%, diabetes, hypertension, obesity, cancer and dementia, due to the sedentary lifestyle imposed by chronic pain and joint stiffening that makes walking difficult or impossible[xi]. So, far from being a benign disease, knee OA must be seen as a serious condition that justifies the relentless search for preventive and curative solutions.

Current treatments **only provide temporary relief of symptoms** (pain and inflammation), but do not stop the progression of the disease at the tissue level. Eventually, surgical joint replacement becomes inevitable and is a highly invasive procedure that exposes the patients to the risk of complications and requires post-operative recovery[xii]. In addition, 20% of patients still experience chronic pain one year after surgery.[xiii]

The therapeutic concept and the medical rationale behind our product is based on the **clinical observation** of one of the world's most renowned rheumatologists, **Prof. Francis Berenbaum** (leading researcher and clinician, former president of OA Research Society International (OARSI))[xiv]) on his OA patients at the Sorbonne St-Antoine University Hospital in Paris, France. He was one of the first clinicians to correlate OA with low-grade inflammation induced by metabolic disorders such as diabetes[xv], his intuition later confirmed by other investigators[xvi]. IHe proposed that drugs targeting metabolic-induced low grade inflammation could become a DMOAD.

Our innovation is based on this major paradigm shift that GLP-1 analogues used in the management of Type-2 Diabetes Mellitus and obesity could be the next game-changing therapeutic solutions for OA. Researchers and clinicians have recognized that the GLP-1 analogue liraglutide, the active pharmaceutical principle in 4P004, indeed has tremendous potential as a broad-spectrum treatment for various age-related diseases, and is currently

in clinical trials for the treatment of neurodegenerative and cardiovascular diseases[xvii].

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