

# Breakthroughs that change patients' lives

Pfizer pre-clinical collaborating interest areas – 2020

Outlined below with application in core research focus areas: oncology, inflammation & immunology, internal medicine and rare diseases. **Non-confidential pre-proposals will be reviewed on a rolling basis from June 1<sup>st</sup> – September 28<sup>th</sup>.**

Opportunities related to **DNA Damage Response and Replicative Stress** such as:

- Chromatin and DNA damage response modulators in the context of nuclear or spatial organization (e.g. biochemical condensates)
- Novel targets identified via synthetic lethal, chemical biology or other approaches, including DNA repair enzymes (esp. nucleases), scaffolding factors and nucleic acid targets (R-loops, G-quadruplexes)
- DNA damage proteins associated with diseases such as cancer and repeat expansion diseases

*Out-of-scope: cell therapies, antibody-drug conjugates, nucleic acid therapeutics*

Opportunities that address the cause or treatment of **Repeat Expansion Diseases**, such as:

- Therapeutic targeting of the mutant gene
- Interventions that halt or reverse the somatic expansion of the repeating DNA sequences
- Novel mechanisms that modulate or regulate the pathological repeat
- Genetic modifiers of repeat instability or repeat contraction

*Out-of-scope: therapeutic approaches that target/clear protein aggregates*

Opportunities to target **Cellular Senescence**, including senolytic and senomorphogenic approaches such as:

- Induction or targeting of senescent-like arrest of tumor cells to overcome drug resistance and/or improve immune response to solid tumors
- Novel senescence targets related to fibrosis, specifically mechanisms responsible for modulating fibroblasts/myofibroblasts function and tissue remodeling by stem/tissue progenitor cells
- Targeting of senescence pathways in tissue resident immune cells in the liver, lung, skin, joints, and gastrointestinal tract that contribute to disease

*Out-of-scope: telomeres/telomerase targeting approaches, age-related dysfunction*

Opportunities related to **Tissue-Immune System Crosstalk** in disease pathology including:

- Targets/pathways that induce immune tolerance by modulation of unique or accessory regulatory cells including macrophages (Mregs), B cells (Bregs), and tolerogenic dendritic cells (tolDCs)
- Novel inflammatory pathways/targets in tissue-resident innate, parenchymal, and stromal cell populations including fibroblasts, stem/tissue progenitors, neutrophils and macrophages

*Out-of-scope: cell and gene therapies*