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 1st – September 28th.**

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 senomomorphic 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

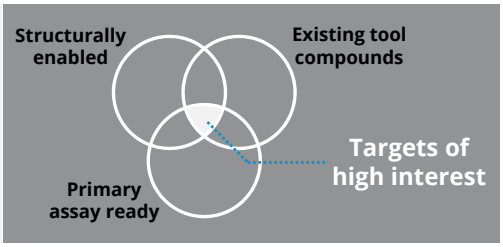
Pfizer's Centers for Therapeutic Innovation

Helpful Tips for Small Molecule Pre-Proposals

Pfizer's Centers for Therapeutic Innovation (CTI) specialize in helping academics bring innovative targets & technologies to patients, but what is it that Pfizer scientists look for in a small molecule pre-proposal? How can you improve the likelihood of success for your pre-proposal?

KEY CONSIDERATIONS

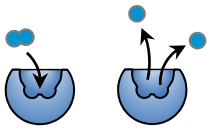
What do Pfizer scientists look for when evaluating small molecule targets?



SMALL MOLECULE AMENABILITY

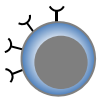
Knowing the target is not necessary but can greatly accelerate drug discovery efforts. Pfizer scientists broadly categorize targets by location, which helps to evaluate small molecule druggability.

Intracellular:



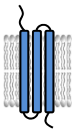
Intracellular targets have proven to be highly druggable. Enzymes such as kinases have been extensively investigated while historically challenging targets such as phosphatases and RNA have more recently shown tractability.

Extracellular/secreted:



Extracellular targets are often the focus of large molecule approaches and differentiation is key. Harnessing intracellularly driven processes such as protein degradation may be challenging.

Membrane bound:



GPCR's and ion channels represent a large percentage of approved small molecule therapeutics. This has been aided by a high level of structural understanding and large number of existing assays.

COMPOUND READY ASSAY

Having a disease-relevant biochemical or cellular assay ready and available is one of the primary means to accelerate the drug discovery process. Collaborators can work with CTI to transfer compounds from Pfizer's internal library for testing, allowing for data generation ahead of any high-throughput-screening or medicinal chemistry.

TOOL COMPOUND

Tool compounds, often with on-target activities in the 1–5 micromolar range, can be instrumental in helping optimize assays and serve as starting points for medicinal chemistry. Whether publicly available or discovered from your in-lab efforts, Pfizer scientists can help to profile existing tools and rapidly identify related compounds from our internal library for follow-up testing.

CRYSTAL STRUCTURE

3D structures are key to helping predict the druggability of a target and can be used to drive both computational screening efforts as well as early medicinal chemistry work. Targets (or homologs) with known structures allow for rational compound design and more targeted screening of Pfizer compound libraries.

If you have any questions that haven't been addressed in this addendum, please ask your technology transfer representative to put you in touch with a small molecule expert from Pfizer and we'd be happy to help guide you through the process.