



Improving Outcomes for Molecularly Defined High Risk Breast Cancer Subgroups

With generous support from B-Search and building on our landmark discovery of 11 molecular defined subgroups of breast cancer with distinct genomic 'drivers' and risks of recurrence (*Nature* 2019, *Nature* 2012), we are developing innovative strategies to diagnose, treat and monitor patients at highest risk of disease progression. Towards this goal, we have established an end-to-end *clinical-translational research platform* that harnesses state-of-the-art experimental and computational methods, spanning patient avatars (organoids) and computer algorithms, to learn and exploit the *unique biology* that underpins high-risk of recurrence breast cancers for therapeutic benefit.

These scientific discoveries, coupled with the infrastructure we have built uniquely position our team to address several of the most pressing challenges in breast oncology. Specifically, we seek to develop and deploy new *diagnostics* and *decision support tools* so that *all* breast cancer patients can receive personalized treatment and monitoring guided by the molecular features of their tumor. We are grateful to partner with B-search to pursue this bold mission at warp speed.

Over the next year we will expand these efforts with several major **milestones** anticipated as well as new directions:

- We will **complete** our Phase IB biomarker stratified clinical trial in high-risk metastatic patients and perform detailed molecular characterization of these patient samples
- We will **launch** our Phase II window-of-opportunity clinical trial to evaluate novel therapeutic strategies in early stage, high-risk of relapse ER+/Her2- patients and to deeply characterize their tumor tissue and blood before and after therapy. This *first in kind* trial advances comprehensive biomarkers in newly diagnosed patients and will be pivotal for the field.
- We will **expand** our biobank of breast cancer patient-derived organoid (PDO) models (40 generated to date) to evaluate the efficacy of established and novel therapeutic agents. Here we leverage the Phase II trial to enrich for patient specimens and organoids representative of the 25% of high-risk of relapse patients for which representative models are urgently needed.
- We will **harness** our growing collection of longitudinal biospecimens from breast cancer patients to develop and evaluate novel methods to monitor and detect recurrence.
- We will **validate** our suite of predictive biomarkers spanning all subgroups of breast cancer in clinical cohorts to enable the translation of these new diagnostic methods.

We are enthusiastic about the rapid progress and momentum we have achieved and the new opportunities that have arisen as a result. This would not have been possible without B-Search support and we are emboldened to accelerate these efforts with renewed support over the following year. This multi-year funding stream will allow us to continue without pause and to retain the best and brightest minds to execute on our bold mission.

Through multiple national and international leadership roles, including as a member of the Board of Directors for the American Association for Cancer Research and an advisor to pharma/biotech, I will champion personalized approaches for breast and other cancers by bringing together key stakeholders across the research, clinical, regulatory, pharmaceutical and advocacy sectors. Breast cancer will be the archetype from which others follow and I am grateful to have this platform at this critical point in time.