March 27, 2024

Dear fellow shareholders,

It is my pleasure to reflect on our accomplishments in 2023 as we continued to solidify our position as the leader in the field of targeted protein modulation and advance the development of our innovative pipeline of promising small molecule and antibody therapeutics in oncology and autoimmune disease. Most importantly, we reported positive clinical data from both of our Bruton's tyrosine kinase (BTK) degrader clinical trials in chronic lymphocytic leukemia (CLL) and non-Hodgkin's lymphoma (NHL). In addition, we advanced our strategic collaborations, which significantly broaden the opportunities and reach of our technology while providing meaningful non-dilutive funding, a key advantage through the bearish biotech equity market during the past year. We continue to translate our deep expertise in E3 ligase biology and our robust DELigase drug discovery platform into the design of promising small molecule drugs that empower the body to fight disease by activating or inhibiting the natural process of protein degradation. Our goal is to develop novel, first-in-class small molecule targeted protein degraders and ligase inhibitors, as well as a whole new class of degrader-antibody conjugate therapies for patients who lack adequate treatment options.

We entered 2023 with important, value-building goals: 1) advance our wholly owned clinical programs to generate data which will guide our late-stage drug development strategy; 2) continue to lead the field with the use of targeted protein modulation through new therapeutic modalities, specifically the development of degrader-antibody conjugates with our new Seagen (now Pfizer) collaboration; and 3) expand the application of our approach into new therapeutic areas with a focus on opportunities in autoimmune disease with Gilead and Sanofi as well as on our own. I am pleased to report that we have been successful on all fronts.

Progress in our clinical programs and plans for the future

Targeted Protein Degradation (TPD) Portfolio: NX-5948 and NX-2127

At the annual meeting of the American Society for Hematology (ASH 2023) in December, we presented promising efficacy and safety data from both of our differentiated BTK degraders, NX-5948 and NX-2127. Nurix continues to be the ground-breaker drug developer for degraders in hematologic malignancies. We see the late entrants of other BTK degraders from larger corporate competitors to be highly validating of our approach, and adding to the excitement in our field.

Our lead TPD program, NX-5948, is an investigational, orally bioavailable, small molecule degrader of BTK that is currently being evaluated in a Phase 1a/b clinical trial in adults with relapsed or refractory B-cell malignancies. Data from the dose escalation stage of the Phase 1 trial of NX-5948 demonstrate dose-dependent pharmacokinetics (PK), resulting in rapid, robust and sustained BTK degradation in all patients treated. NX-5948 was well-tolerated across all doses with a favorable safety profile demonstrated thus far. Remarkably, preliminary efficacy data from this heavily pretreated population demonstrated clinical benefit in six of seven patients with CLL even at initial dose levels of dose escalation. Durable responses were seen in NHL patients, with almost half the patients continuing to receive treatment as of the data cut-off date.

In January 2024, the FDA granted Fast Track designation for NX-5948 for the treatment of adult patients with relapsed or refractory CLL or small lymphocytic lymphoma after at least two lines of therapy, including a BTK inhibitor (BTKi) and a B-cell lymphoma 2 (BCL2) inhibitor. The FDA's Fast Track designation is intended to facilitate and expedite the development and review of drug candidates to treat serious conditions and fulfill an unmet medical need. The value of this designation, particularly in light of our emerging development plans for NX-5948 in CLL, is that we may be eligible for more frequent interactions with the FDA to discuss the candidate's development and, if relevant criteria are met, NX-5948 may be eligible for Accelerated Approval and Priority Review.

NX-5948 has another differentiating feature that potentially expands its therapeutic utility. As we have demonstrated in preclinical models, NX-5948 can cross the blood brain barrier and degrade BTK in brain resident lymphoma cells and microglia. In addition, we have generated preclinical data in animal models for rheumatoid arthritis and multiple sclerosis that demonstrate its therapeutic potential in autoimmune disease. Autoimmune disease is a therapeutic area of increasing focus for us and we are expanding our non-clinical studies of NX-5948 to enable an investigational new drug (IND) application for NX-5948 in autoimmune indications.

Our second program currently in patients with r/r B-cell malignancies, NX-2127, is an orally bioavailable degrader of BTK with immunomodulatory activity. At ASH 2023, we presented data from our Phase 1a/b clinical trial of NX-2127, which includes three Phase 1b expansion cohorts in patients with diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL) and CLL. NX-2127 exhibited dose-dependent PK, leading to robust and sustained degradation of BTK and biologically relevant degradation of IKZF1 (Ikaros). Treatment with NX-2127 in CLL resulted in rapid and durable responses in the heavily pre-treated patient population including patients with BTKi resistance mutations. Durable, complete responses were reported in two patients with DLBCL and MCL, which remained ongoing for over one year. NX-2127 had a manageable safety profile that was consistent with previous reports for BTK-targeted and immunomodulatory therapies. Screening and enrollment of new study participants had been paused at the end of 2023 due to a partial clinical hold placed on the study following the company's communication to the FDA of its intention to transition to an improved manufacturing process. The FDA has now lifted the partial clinical hold, which enables us to introduce drug product manufactured with the improved process into the ongoing Phase 1 clinical trial. We expect to resume the enrollment of new patients in the near future.

We have always believed that BTK degradation is a superior approach to inhibition with the potential to address the growing problem of acquired resistance mutations to current BTK therapies leading to disease recurrence in patients. In February this year, we published data in the high impact, international journal *Science* describing the elucidation of a previously unappreciated oncogenic scaffold function of BTK, which is also responsible for clinical resistance to enzymatic inhibitors. The data also show that NX-2127, and by extension potentially NX-5948, can overcome this resistance across a broad range of acquired mutations, reinforcing the broad utility of the targeted protein degradation mechanism to more completely block BTK function as compared to inhibition approaches. These data, and our growing body of clinical data, highlight the potential of degraders to become the next dominant class of agents in the valuable BTK-targeted therapy market.

Targeted protein elevation: NX-1607

The lead drug candidate in our targeted protein elevation portfolio, NX-1607, is an orally bioavailable inhibitor of the E3 ligase Casitas B-lineage lymphoma proto-oncogene B (CBL-B), which normally degrades proteins in cells of the immune system. This novel inhibitor approach is a first-in-class compound, and we are developing it for immuno-oncology indications, including a range of solid tumor types and lymphoma. Nurix was the first to establish the ability to screen this target and identify inhibitors to this ligase, enabling the elevation of levels of the proteins CBL-B controls in immune cells to enhance the anti-tumor immune response. Importantly, our early clinical data demonstrated biomarker-based evidence of CBL-B inhibition in patients. We are evaluating NX-1607 in an ongoing, Phase 1 trial in adults in a range of solid tumor types and lymphoma as a monotherapy and in a combination cohort with paclitaxel.

Preclinical Pipeline

We have a robust preclinical pipeline of both wholly owned assets and those we are developing with our strategic collaborators Gilead, Sanofi, and most recently, Pfizer. In March 2023, Gilead exercised its option to exclusively license Nurix's investigational IRAK4 targeted protein degrader development candidate for rheumatoid arthritis and other inflammatory diseases. This important milestone provided clear evidence of the steady progress that we have been making in our strategic collaborations, which enable us to advance multiple degrader programs in addition to our wholly owned programs, and highlights the growing value of our platform to create medicines to address therapeutic areas in addition to oncology. In 2024, we plan to select another new targeted protein degrader development candidate and provide information on its therapeutic area and development plans.

Corporate and business development progress

In September of 2023, we announced a multi-year, multi-target agreement with Seagen (now Pfizer) to discover, develop, and commercialize a new class of medicines called Degrader-Antibody Conjugates (DACs). This exciting collaboration focuses on an innovative approach to combine two powerful technologies to target cancer—antibody-drug conjugation (ADC) and targeted protein degradation (TPD)—with the goal of creating a new class of antibody therapeutics.

Overall, our strategic collaborations generated meaningful non-dilutive funding of $100 million in 2023, which includes a $60 million upfront payment from Seagen and $40 million in success-based milestones and licensing fees from Gilead and Sanofi. This funding positions us well financially to progress and expand our pipeline through important milestones in 2024 and beyond and realize the broader potential value of our platform to create medicines to address therapeutic areas in addition to oncology, such as autoimmune diseases.

2024 Outlook

2024 is shaping up to be an exciting, data-rich year for Nurix. Recent data from our BTK degrader programs has helped us to understand where these two powerful degraders can advance into the B cell lymphoma treatment landscape and potentially displace BTK inhibitors. We are prioritizing expansion of NX-5948 in CLL following the dose escalation portion of that study, and we believe that the dual activity of NX-2127 will prove advantageous in NHL in indications such as DLBCL and MCL, where we have already observed durable complete responses.

In 2024, we expect to define doses for NX-5984 Phase 1b cohort expansion in CLL and NHL, and we are accelerating enrollment to enable pivotal trials. We look forward to presenting additional clinical data with higher dose levels and longer treatment duration mid-year. We also expect to complete ongoing preclinical studies that can enable an investigational new drug (IND) application for NX-5948 in autoimmune indications. In our NX-1607 program we expect to present data from the Phase 1a dose-escalation portion of the trial of and to define dose(s) to enable Phase 1b cohort expansion. Additionally, we plan to select a new targeted protein degrader molecule for development from our research pipeline, and to continue to make meaningful progress in our strategic collaborations.

We intend to maintain the momentum we have built as we continue to advance our wholly owned clinical programs and collaboration pipeline and continue to expand into inflammatory diseases while maintaining fiscal discipline and prudent use of our cash resources. Our goal remains to develop life-changing drugs for patients with significant unmet medical needs. I look forward to keeping you apprised of our progress.

Thank you for your continued support.

Sincerely,

Arthur T. Sands, M.D., Ph.D.
President, Chief Executive Officer and Board Member