

### TO THE SHAREHOLDERS OF NANOBIOTIX S.A. AND NANOBIOTIX CORP.,

Whenever you are in pursuit of delivering novel innovation with the potential to improve the lives of millions of patients, every year is pivotal. From that perspective, 2023 was simply the twentieth step on the path to realizing the promise of our nanophysics-based approach to therapeutic development for patients with cancer and other major diseases.

Nanobiotix has long been known for our lead product candidate, potential first-in-class radioenhancer NBTXR3. The hypothesis that drives the NBTXR3 clinical development program is that by injecting biologically-inert, electron-dense nanoparticles directly into solid tumors, we can create an up-to nine-fold increase in the dose of radiation therapy delivered to the target tumor without increasing the dose in surrounding healthy tissues. With positive results from a randomized Phase 2/3 results that led to regulatory approval for the treatment of patients with soft tissue sarcomas in Europe; recently reported positive Phase 1 final and exploratory results in locally advanced head and neck cancer ("LA-HNSCC"); and an ongoing Phase 3 LA-HNSCC study in a similar patient population to the positive Phase 1—it is no wonder that NBTXR3's potential to control locally advanced solid tumors has driven the excitement, anticipation, and expectations for Nanobiotix for much of our history. The licensing agreement we signed with Janssen Pharmaceutica NV ("Janssen"), a Johnson & Johnson company, in July of 2023 stands as a testament to the hard work of our team and NBTXR3's practice-changing potential in oncology.

From another perspective, NBTXR3 is not only paving the way for a new therapeutic class in cancer treatment, but also laying the groundwork for a new era of nanophysics throughout the healthcare industry driven by the discovery, design, development, and manufacture of nanoparticle-based therapies. NBTXR3, as the first product candidate from our first nanotechnology platform, could provide the first large-scale proof of this concept, but the radioenhancer is only the beginning. Today's focus with our new partner is to secure the path to market for NBTXR3, but the time has come for Nanobiotix to begin expanding the impact of nanoparticle-based therapies in healthcare.

To that end, our corporate strategy is to develop three nanotechnology platforms in sequence: first commercializing NBTXR3 to achieve financial sustainability and allow for further advancement of the second platform, Curadigm, and third platform, Oocuity. Curadigm's platform has enabled the discovery of a "nanoprimer" designed to temporarily occupy the liver cells responsible for clearing therapeutics from the blood stream after intravenous ("IV") administration. This mechanism aims to prime the body to increase the availability of therapeutics in the blood which can then treat the target disease. Our view is that the Curadigm platform presents attractive partnership and collaboration opportunities across drug classes, particularly with RNA-based therapies. The Oocuity platform aims to bring our nanophysics-based therapeutic approach to another area that has challenged the healthcare industry since its inception: neurological disease. The platform is based on the principle that nanoparticle materials can interact with and influence neuronal networks via their electrical properties. We expect our hard work on these three platforms, and the strong intellectual property



underpinning them, to sustain and expand the Nanobiotix presence in the biopharmaceutical industry for the long term.

Advancing disruptive innovation in healthcare will always involve a balance between positioning for the future while staying firmly rooted in the present. The global biopharmaceutical industry continues our collective march toward the so-called "patent cliff" in the next decade, with many "new" drugs facing market competition from generics. Over the next few years, demand for novel technologies with strong intellectual property protections and the potential to deliver multiple transformative, potential first-in-class therapeutic agents is poised to grow exponentially. We believe that our pioneering leadership in nanoparticle-based therapies will present a world of opportunity in this environment.

More importantly, however, our primary responsibilities are to improve treatment outcomes for patients and create value for shareholders. With 2023 behind us and 2024 underway, our focus remains on bringing NBTXR3 to market by executing our global alliance and maintaining financial discipline.

#### **Bringing NBTXR3 to Market**

Our global licensing agreement with Janssen and the alliance it has established provide a road map to the bright future we expect for NBTXR3. The near-term objectives of the alliance are to achieve global registration of NBTXR3 for the treatment of elderly patients with LA-HNSCC through the completion of ongoing pivotal Phase 3 study NANORAY-312, and to launch a Phase 2 study evaluating NBTXR3 for the treatment of patients with stage III non-small cell lung cancer ("NSCLC"). We are well under way with our allocation of the \$30 million upfront payment to Nanobiotix, \$30 million invested through equity financing from Johnson & Johnson Innovation – JJDC, Inc. ("JJDC"), and \$20 million milestone payment for operational milestones achieved in NANORAY-312, to the preparation of the pivotal trial for a successful regulatory submission in the event of positive results at interim analysis and to the launch of the new lung cancer program. The licensing agreement also includes a framework for five new indications that may be developed by Janssen at its sole discretion as well as additional indications that may be developed by Nanobiotix in alignment with Janssen.

To ensure we are prepared to move quickly into later stage development of indications beyond LA-HNSCC and stage III NSCLC, Nanobiotix continues to lead a Phase 1 cancer immunotherapy program in the United States ("US") and collaborate with The University of Texas MD Anderson Cancer Center ("MD Anderson") on several early-stage studies evaluating NBTXR3 alone and in combination with other therapeutic agents and treatment modalities. We expect to provide an update from the immunotherapy program, evaluating the potential for radiotherapy-activated NBTXR3 to improve the therapeutic response to cancer immunotherapy agents such as immune checkpoint inhibitors, at a medical congress in the first half this year. Taken together with the ongoing Phase 1 and Phase 2 studies at MD Anderson—our evaluation of NBTXR3 in pancreatic cancer in particular—and the positive early data we have observed in other indications such as liver cancer and prostate cancer, we believe Nanobiotix is well positioned to rapidly expand NBTXR3 development in the coming years.



### **Executing the NBTXR3 Global Alliance**

Every decision in the 20-year history of Nanobiotix has been taken with the sole intent of maximizing the long-term potential impact of nanoparticle-based therapeutics for as many patients with major diseases as possible. From the outset we understood that, with a totally new approach to designing and developing therapeutic agents, it would take more than simply generating data showing that our first product candidate had the potential to outperform both the standard of care and competitive agents in terms of safety and efficacy. We would need to help investors, regulators, and potential industry partners develop a framework for evaluating the potential of our new technologies against other therapies. Moreover, we would also need to ensure that our non-traditional therapeutics could deliver soundly on the traditional metrics and conventions expected for commercial assets in the global healthcare industry.

Bringing a therapeutic candidate from concept to global registration is a daunting proposition for any biotech company, even those working within well-known asset classes with well-worn development and regulatory pathways. The level of difficulty increases even further when you are developing a novel innovation like NBTXR3, and that is why our collaboration with Janssen is great news for patients, for healthcare professionals, and for all other supporters of our radioenhancer's potential. Our strategic alliance, governed by a Joint Steering Committee comprised equally of executives from both companies, is prioritizing the preparation of our randomized Phase 3 study, NANORAY-312, for regulatory submission in the event of a positive interim analysis. This process includes ensuring that the study operations, data collection procedures, and manufacturing procedures are consistent with Janssen's traditional approach for late-stage strategic assets. We are confident that their support will optimize the probability of success for our first global regulatory approval.

# **Maintaining Financial Discipline**

In 2023, we continued to experience generally unfavorable macroeconomic conditions surrounding the biotechnology industry. Investors remained reluctant to deploy capital in the face of rising inflation and high interest rates, and key indices tracking the biotech sector in the US and Europe neared record lows. Although so far in 2024 we have seen a groundswell of optimism flow back into the sector, driven at least in part by a potential change in posture from central banks and tailwinds in the broader technology and biopharmaceutical sectors, this rapid change in sentiment simply serves to illustrate the unpredictable volatility inherent to our industry.

At Nanobiotix, our approach has been to maximize long-term value by controlling what we can control—the integrity of our science, the efficiency of our operations, and the quality of our relationships with our shareholders and other financial partners. Despite a challenging market, Nanobiotix was able to improve our fiscal outlook at year-end 2023 compared to the end of 2022. By controlling operating expenses; removing the cash covenant in our financing agreement with the European Investment Bank; executing our global license agreement with Janssen; closing an equity raise with highly reputable investors; and achieving the first operational milestone



outlined in the Janssen licensing agreement, we ended 2023 with operating runway into the third quarter of 2025 compared to year-end 2022 when we had operating runway into the third quarter of 2023.

These financial accomplishments evidence the potential value the biopharmaceutical industry at-large sees in our technology, along with the tremendous faith and confidence our investors and other financiers hold in our vision and our management. We understand that faith and confidence do not last forever, and that the only path to the impact we want to have on the world is through the sustainable financing that comes from commercial revenue. With that in mind, we remain exceedingly grateful to all those who have and continue to support our mission to revolutionize treatment for millions of patients around the world. Our longstanding commitment to reward that trust by delivering medical value for patients and economic value for shareholders guides every action we take.

# **Revolutionizing Healthcare**

In Clayton Christensen's *The Innovator's Dilemma: When New Technologies Cause Great Firms to Fail*, Christensen concludes that successful companies can do everything "right" and still lose their market leadership if they are unable to recognize and incorporate disruptive innovation. For most of our 20-year history, Nanobiotix has stood on the other side of this problem. Equipped with a truly novel approach, we have worked tirelessly to blaze the necessary trails for patients around the world to realize the potential of nanoparticle-based therapeutics.

As we move toward potential global registration of NBTXR3 and unveil the equally disruptive potential of Curadigm and Oocuity, we expect nanoparticle-based therapies to emerge as a revolutionary new mainstream treatment modality. And for the next 20 years and beyond, we expect Nanobiotix to lead the revolution.

Thank you,

Laurent Levy

Chief Executive Officer and Chairman of the Executive Board at Nanobiotix