volume is based on percentage of gross tumor volume (GTV), as determined per central review. The primary objective is to determine the RP2D of R3/RT/PD-1. The secondary objectives are to evaluate the anti-tumor response (objective response rate; ORR) of R3/RT/PD-1, the safety and feasibility of NBTXR3 injection, and the body kinetic profile of NBTXR3. Exploratory objectives will assess biomarkers of response to R3/RT/PD-1, including PD-L1 status by IHC, as well as mRNA and cytokine immune marker profiling.

Clinical trial identification: NCT03589339.

Legal entity responsible for the study: Nanobiotix, SA.

Funding: Nanobiotix, SA.

Disclosure: C. Shen: Honoraria (self): Nanobiotix. K. Jameson: Full / Part-time employment: Nanobiotix. J. Weiss: Honoraria (self): Nanobiotix. T. Hackman: Honoraria (self): Nanobiotix. D. Corum: Full / Part-time employment: Nanobiotix. J.A. Akulian: Honoraria (self): Nanobiotix. R. Dixon: Honoraria (self): Nanobiotix. A. Pearson: Honoraria (self): Nanobiotix. J. Frakes: Honoraria (self): Nanobiotix. P. Said: Full / Part-time employment: Nanobiotix. H. Miraoui: Full / Part-time employment: Nanobiotix. E. Baskin-Bey: Full / Part-time employment: Nanobiotix. T. Seiwert: Honoraria (self): Nanobiotix.

126TiP A phase I study of NBTXR3 activated by radiotherapy for patients with advanced cancers treated with an anti-PD-1 therapy

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Background: The majority of cancer patients are resistant to immune therapy; only around 15% respond to immune checkpoint inhibitors (ICI). Thus, strategies able to increase ICI response are of great interest. Recent work suggests radiotherapy (RT) can act as an immunomodulator to increase the proportion of ICI responders and improve clinical outcomes. However, RT dose and ultimate efficacy are limited by toxicity related to exposure of healthy tissues. NBTXR3 is a first-in-class radioenhancer administered by intratumoral injection, designed at the nanoscale to increase RT energy dose deposition within the tumor. The result is increased radiation-dependent tumor cell killing, without increasing radiation exposure of healthy tissues. Preclinical and early clinical data suggest NBTXR3 activated by RT can increase the anti-tumor immune response, producing both local and systemic (abscopal) effects. We hypothesize that NBTXR3 activated by RT, in combination with anti-PD-1 therapy (R3/RT/PD-1), will act synergistically to maximize the local RT effect while also producing a systemic response sufficient to increase the proportion of ICI responders or convert ICI non-responders to responders.

Trial Design: The NANORAY-1100 study is a multicenter, open-label, phase I study that aims to evaluate the safety and tolerability of R3/RT/PD-1 in three cohorts of participants with either: (1) Locoregional recurrent (LRR) or recurrent and metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) amenable to re-irradiation of the head and neck (HN) field, (2) Lung metastases originating from any primary cancer eligible for anti-PD-1 therapy, or (3) Liver metastases originating from any primary cancer eligible for anti-PD-1 therapy. Participants will be enrolled such that approximately two-thirds of each cohort will be anti-PD-1 non-responders. NBTXR3 injection