

# Phase 1 Study of Intratumoral Administration of JNJ-87704916, an Oncolytic Virus, as Monotherapy and in Combination with Cetrelimab in Advanced Solid Tumors

Victor Moreno<sup>1</sup>, Emiliano Calvo<sup>2</sup>, Liza C. Villaruz<sup>3</sup>, Enriqueta Felip<sup>4</sup>, Rastislav Bahleda<sup>5</sup>, Christopher Manley<sup>6</sup>, Ester Garcia-Lorenzo<sup>1</sup>, Ramon Yarza<sup>2</sup>, Juan Jose Soto-Castillo<sup>2</sup>, Aisha Hasan<sup>7</sup>, Julia Billiard<sup>7</sup>, Jorge Da Silva<sup>7</sup>, Ariel Chen<sup>7</sup>, Douglas Steinbach<sup>7</sup>, Samantha Weber<sup>7</sup>, Samaan Rafeq<sup>7</sup>, Rajesh Bandekar<sup>7</sup>, Boting Ning<sup>7</sup>, Stewart Bates<sup>7</sup>, Roland Knoblauch<sup>7</sup>, Sarina A. Piha-Paul<sup>8</sup>

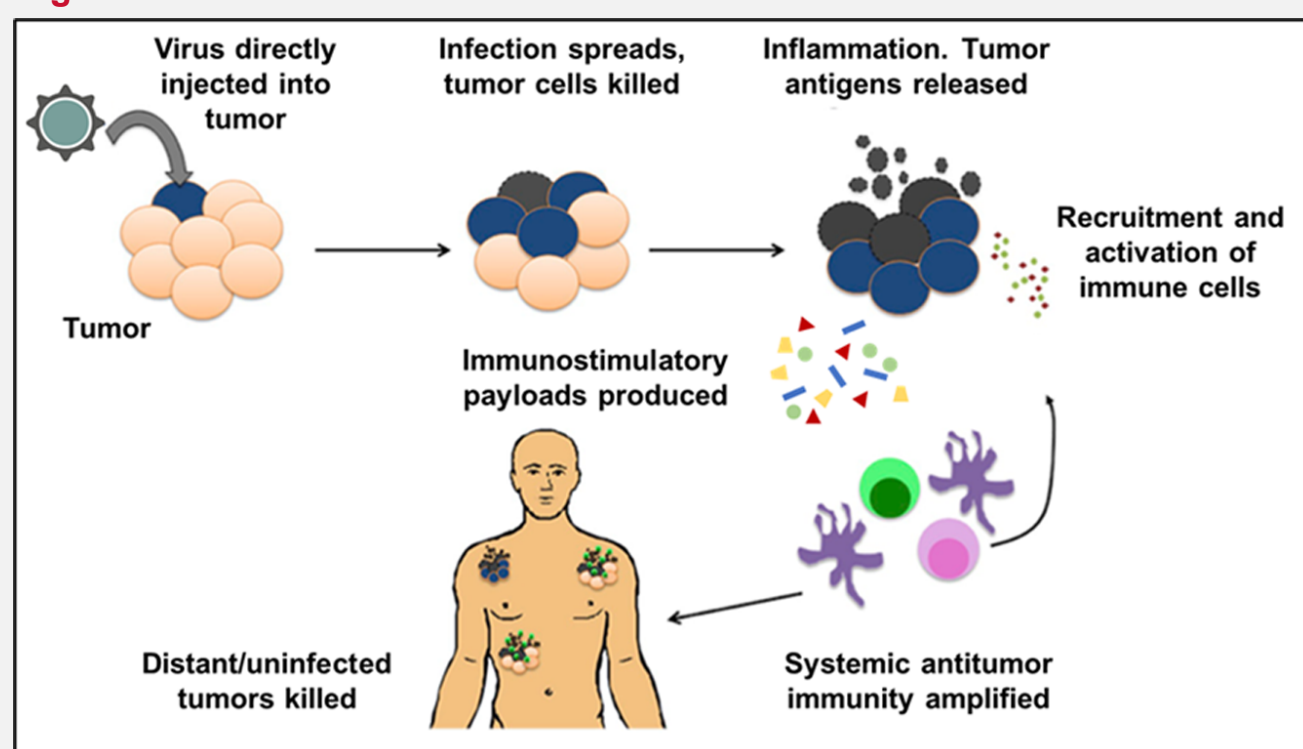
<sup>1</sup>START-FJD, Fundación Jimenez Diaz, Madrid, Spain; <sup>2</sup>START-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; <sup>3</sup>UPMC Hillman Cancer Center, Pittsburgh, PA, USA; <sup>4</sup>Vall D'Hebron Institute of Oncology, Barcelona, SPAIN; <sup>5</sup>Gustave Roussy, Paris, FRANCE; <sup>6</sup>Fox Chase Cancer Center, Philadelphia, PA, USA; <sup>7</sup>Johnson & Johnson, New Brunswick, NJ, USA; <sup>8</sup>University of Texas, MD Anderson Cancer Center, Houston, TX, USA  
Study sponsored by Johnson & Johnson

## BACKGROUND

- While immune-oncologic therapies (IO) have transformed the treatment of non-small cell lung cancer (NSCLC), only a minority of patients experience profound clinical benefit. Attempts to further improve outcomes with systemic IO therapies have been limited by toxicity.
- JNJ-87704916 (JNJ-4916), an HSV-1-based oncolytic virus, seeks to overcome this limitation through intratumoral delivery and expression of 4 immunomodulatory payloads (FLT3L, CD40 agonist, anti-CTLA4, and IL-12) to enhance all stages of the anti-tumor immune response.
- The HSV-1 platform was leveraged to preferentially replicate in tumor cells with modifications that enable prolonged persistence within tumors (Figure 1).<sup>1</sup>

**JNJ-4916 is an oncolytic virus designed to induce and sustain systemic immune responses through intratumoral injection.**

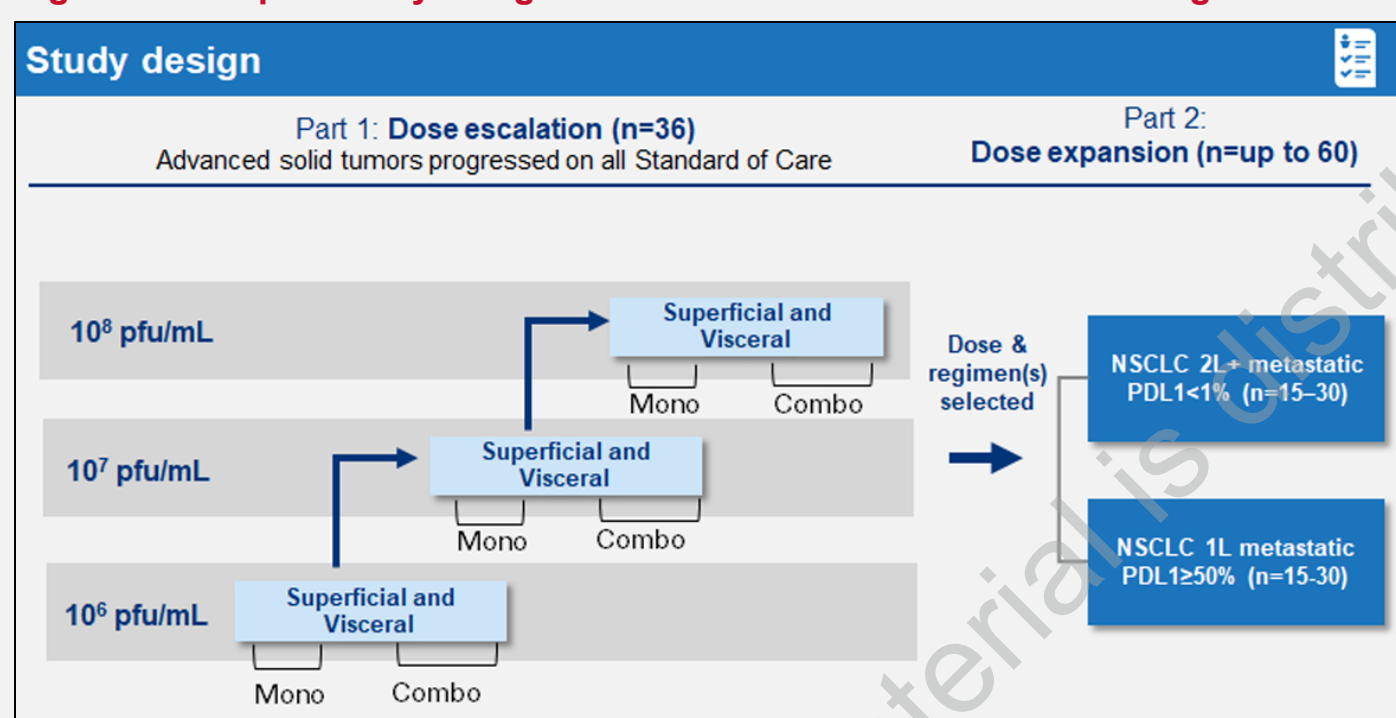
Figure 1. Macro-level HSV-1 mechanism of action



## METHODS

- The FIH 87704916LUC1001 study is characterizing the safety and preliminary efficacy of increasing doses of intratumorally delivered JNJ-4916 in participants (pts) with advanced solid tumors, with the goal of identifying the recommended dosing in combination with cetrelimab, an anti-PD1 antibody.
- The Phase 1 study is a multicenter 2-part study, consisting of dose escalation (Part 1) followed by dose expansion (Part 2) (Figure 2), with reported results for Part 1.
- The study is being conducted at 7 sites in the USA, Spain, and France.
- Part 1 enrolled pts with advanced solid tumors evaluating 3 dose levels to determine a safe and feasible dose of JNJ-4916 in combination with cetrelimab with ongoing evaluation to develop the combination dose.
- The safety of JNJ-4916 as monotherapy (q2W), and in combination with cetrelimab (q4W; initiated with the second dose of JNJ-4916), was evaluated in sequential 14-day DLT periods in individual participants. Superficial and/or visceral lesions were administered 0.5–10 mL, based upon lesion diameter; multiple lesions could be dosed, up to 10 mL total.
- Pharmacological evaluations included quantification of payload expression in serum and tumor biopsies.
- Efficacy was evaluated through CT scans using RECIST v1.1 criteria separately for injected and uninjected lesions response.

Figure 2. Two-part study design to determine safe and feasible dosing of JNJ-4916



1L, frontline therapy; 2L+, second or higher line of therapy; PDL1, programmed cell death ligand 1; PFU, plaque forming units

## Participant Characteristics

- As of the data cutoff, 7 Mar 2025, among the 22 pts dosed, 146 JNJ-4916 doses were administered in 97 procedures.
- Injected lesions were predominantly viscera located (85%), most frequently in the liver (45%) (Table 1). Doses ranged from 0.5 mL up to the maximum of 10 mL per treatment.
- Participant characteristics were:
  - Median age: 63 years (34; 83)
  - Sex: 14 females and 8 males
  - Received 1–10 prior lines of therapy
  - Majority with cold tumor types, except 1 NSCLC and 3 melanoma
- 40 unique lesions were injected (35 visceral, 5 superficial).

Table 1. Lesion location: all study doses (N=146)

| Location              | n  |
|-----------------------|----|
| Liver                 | 65 |
| Lymph node            | 22 |
| Abdominal wall        | 17 |
| Lung                  | 10 |
| Chest wall            | 9  |
| Peritoneum            | 8  |
| Pelvis                | 6  |
| Kidney                | 3  |
| Pancreas              | 3  |
| Iliac                 | 2  |
| Right inguinal lesion | 1  |

## Safety

- Overall, the combination of JNJ-4916 and cetrelimab was well tolerated (Table 2).
- The majority of toxicities were of Grade 1–2 severity, with the following ≥Grade 3: 4 JNJ-4916-related in 1 pt (Gr 3 viremia, ulcerative keratitis, ALT increase, and Gr 4 AST increase); 3 cetrelimab-related in 1 pt (Gr 3 myocarditis, cardiac failure and glomerulonephritis), and 2 procedure-related in 1 pt (Gr 3 hemoperitoneum) and anemia).

Table 2. Most frequently reported (≥15%) TEAEs

|  | JNJ-4916 10 <sup>6</sup> PFU/mL Q2W+CET Q4W | JNJ-4916 10 <sup>7</sup> PFU/mL Q2W+CET Q4W | JNJ-4916 10 <sup>8</sup> PFU/mL Q2W+CET Q4W | Total      |
|--|---|---|---|------------|
| Analysis set: All treated                | 6   | 6   | 10  | 22         |
| Participants with 1 or more TEAEs, n (%) | 6 (100.0)                                   | 6 (100.0)                                   | 10 (100.0)                                  | 22 (100.0) |
| Preferred term, n (%)                    |   |   |   |            |
| Anaemia                                  | 4 (66.7)                                    | 2 (33.3)                                    | 4 (40.0)                                    | 10 (45.5)  |
| Pyrexia                                  | 3 (50.0)                                    | 2 (33.3)                                    | 5 (50.0)                                    | 10 (45.5)  |
| Arthralgia                               | 2 (33.3)                                    | 0 (0.0)                                     | 4 (40.0)                                    | 6 (27.3)   |
| Nausea                                   | 1 (16.7)                                    | 1 (16.7)                                    | 4 (40.0)                                    | 6 (27.3)   |
| Fatigue                                  | 2 (33.3)                                    | 1 (16.7)                                    | 2 (20.0)                                    | 5 (22.7)   |
| Hyponatraemia                            | 4 (66.7)                                    | 1 (16.7)                                    | 0 (0.0)                                     | 5 (22.7)   |
| Musculoskeletal chest pain               | 3 (50.0)                                    | 1 (16.7)                                    | 1 (10.0)                                    | 5 (22.7)   |
| Dyspnoea                                 | 3 (50.0)                                    | 0 (0.0)                                     | 1 (10.0)                                    | 4 (18.2)   |
| Headache                                 | 2 (33.3)                                    | 1 (16.7)                                    | 1 (10.0)                                    | 4 (18.2)   |

CET, cetrelimab; Q2W, biweekly; Q4W, every 4 weeks; PFU, plaque forming units; TEAE, treatment-emergent adverse event

## RESULTS

### Treatment Duration, Response, & Payload Levels

- Multiple biweekly injections were safe and feasible, with up to a maximum of 13 doses administered to pts (Figure 3).
- Payloads were detected in tumor biopsies obtained from all 6 pts assessed 48–72 h post first injection (Figure 4). Results of payloads monitoring in serum are shown in Figure 5.

Figure 3. Duration of treatment as of data cut-off: 7 Mar 2025

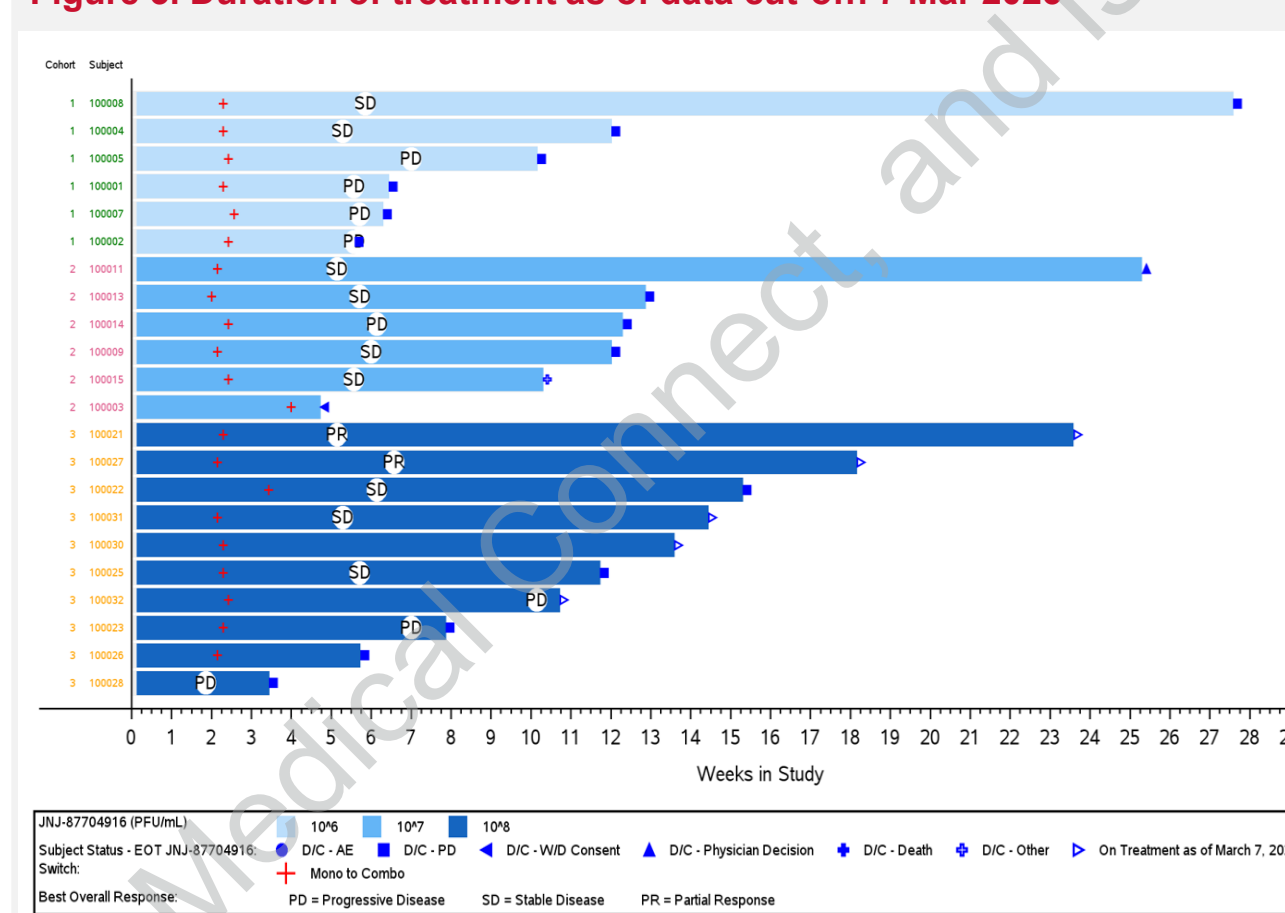
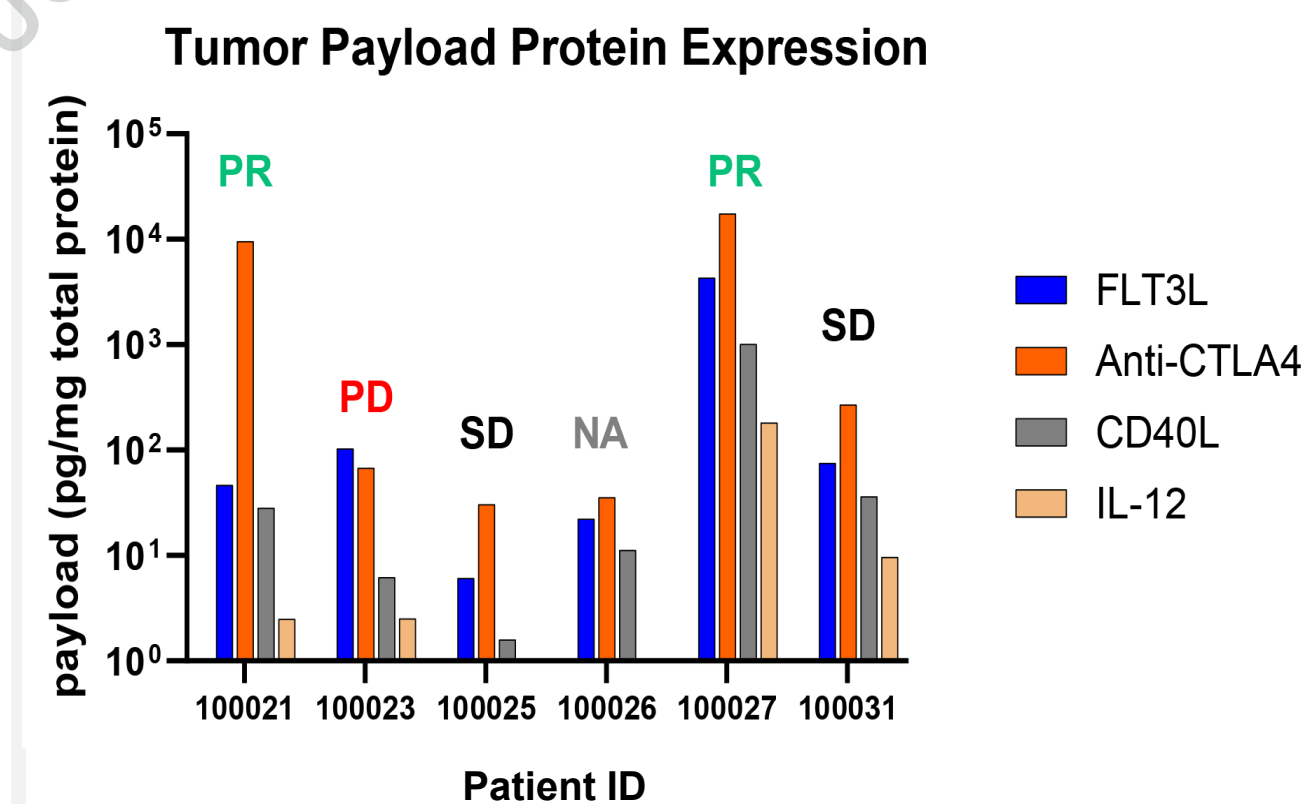
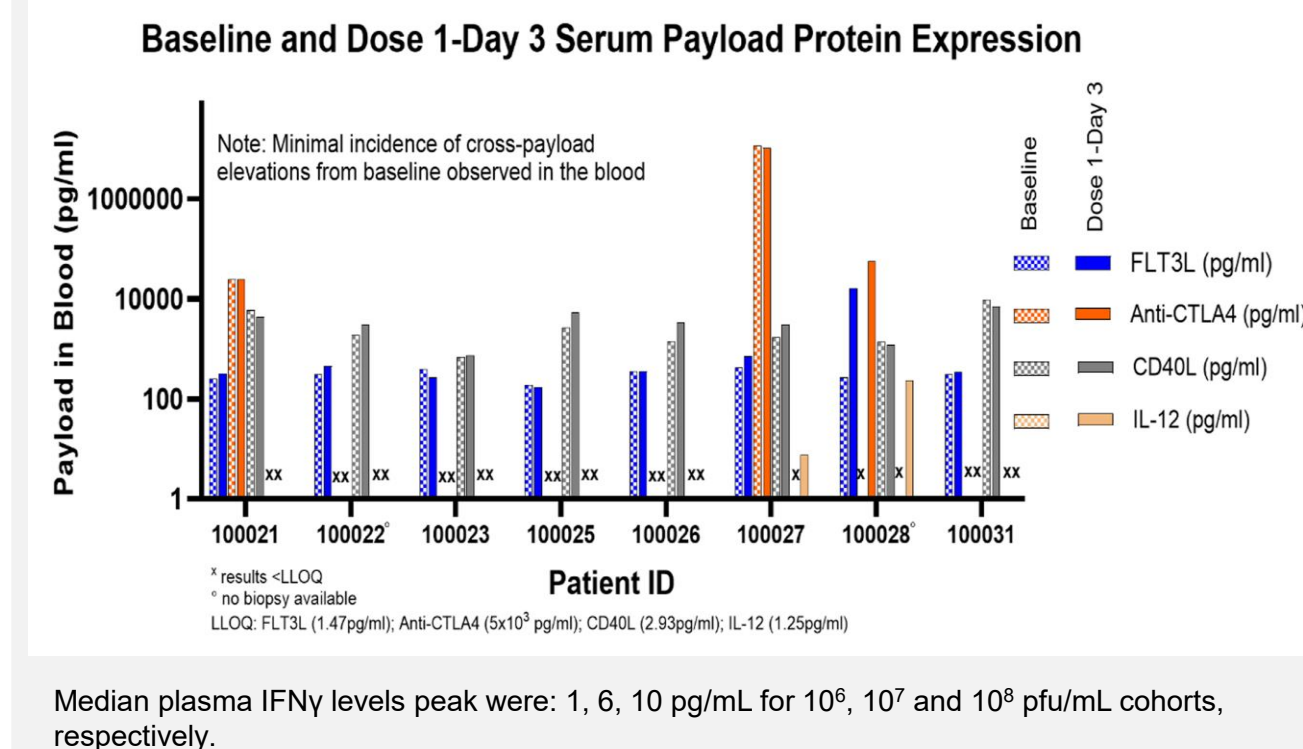


Figure 4. Tumor biopsies were obtained in 6 pts with detected presence of 4 payloads. Best response achieved in each pt is also shown.



NA, not available; PD, progressive disease; PR, partial response; SD, stable disease

Figure 5. Blood serum payload expression in 8 pts at the highest (10<sup>8</sup> PFU/ml) dose as of the 7 Mar 25 data cutoff, shown at baseline and on day 3 following the first dose. There were minimal blood serum elevations for all payloads.

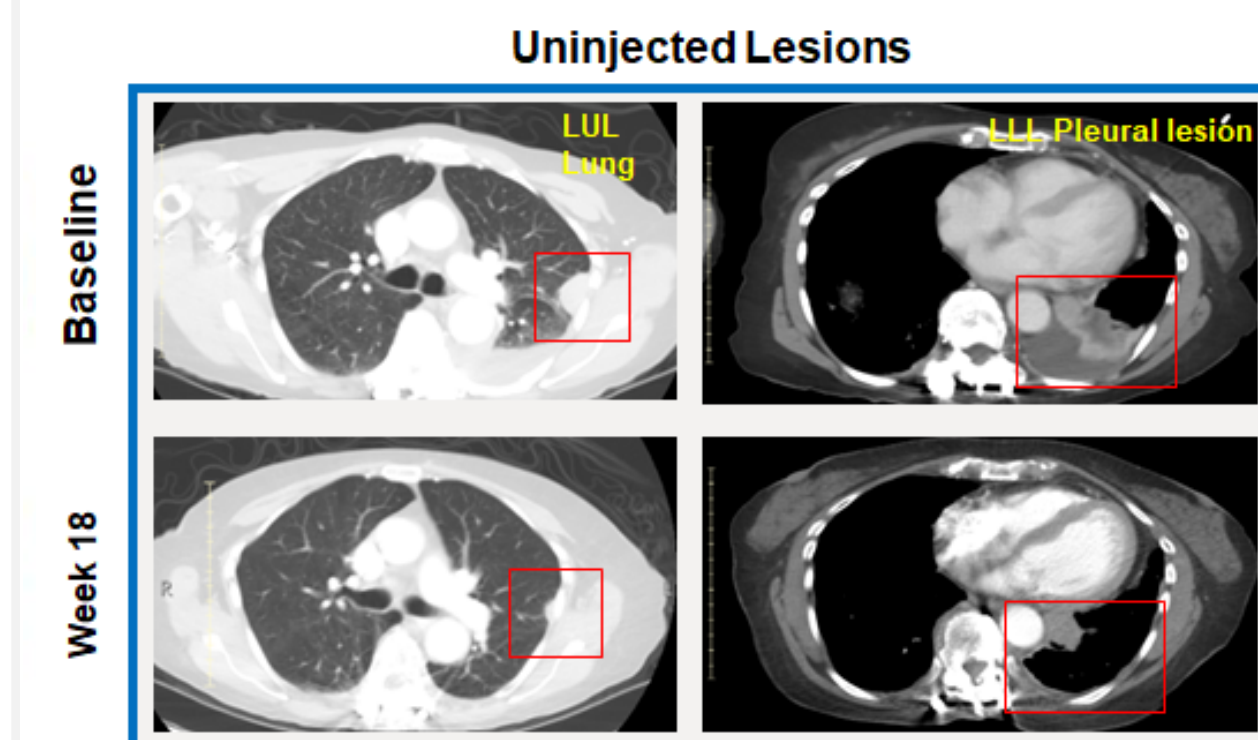
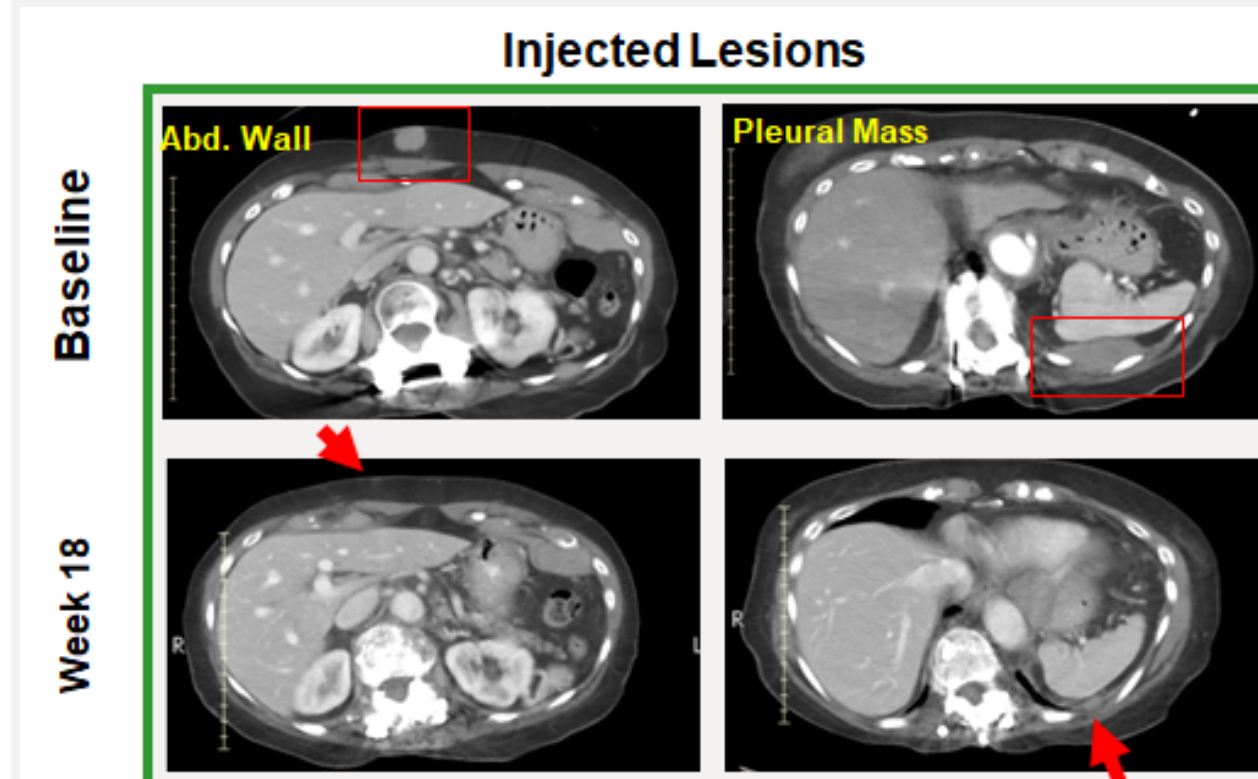


Median plasma IFN $\gamma$  levels peak were: 1, 6, 10 pg/mL for 10<sup>6</sup>, 10<sup>7</sup> and 10<sup>8</sup> pfu/mL cohorts, respectively.

### Objective Partial Response

- Two (2) pts in the 10<sup>8</sup> PFU/mL cohort, each with melanoma previously refractory to anti-PD-(L)1 therapy, have shown RECIST defined Partial Responses, with tumor regression in both injected and uninjected lesions (Figure 6).

Figure 6. Overall PR of -55% observed at 18 weeks in a 79-year-old female with melanoma refractory to immune therapy who received the top dose: PR of -73% and -54% in injected lesions (top panels) and -59% in uninjected lesions (bottom panels).



## CONCLUSIONS

- The recommended dose of JNJ-4916 to advance to expansion cohorts was determined to be 10<sup>8</sup> PFU/mL with demonstrated safety and tolerability of biweekly dosing in advanced solid tumors.
- Safety and feasibility of repeated visceral injections demonstrated in pts with advanced cancer, with partial responses in 2 pts with primary IO resistant melanoma.
- Proof-of-concept demonstrated with expression of payloads detected in 6/6 sampled tumors at the 10<sup>8</sup> PFU/mL dose level in part 1 with limited systemic exposure.
- Payload detection demonstrates repeatable intratumoral pharmacokinetics with low levels in systemic circulation.
- JNJ-4916 induced a dose-dependent, transient increase in plasma IFN $\gamma$  levels.
- Part 2 expansion in 1L and 2L+ NSCLC is actively enrolling pts concurrently with continued dose development in Part 1.

**ABBREVIATIONS**  
1L, frontline therapy; 2L+, second or higher line of therapy; CD40L, CD40 agonist; CET, cetrelimab; CT, computed tomography; CTLA4, cytotoxic T-lymphocyte-associated protein 4; DLT, dose-limiting toxicity; FLT3L, Fms-like tyrosine kinase 3 ligand; HSV, herpes simplex virus; IL-12, interleukin 12; IO, immune-oncologic; NA, not available; NSCLC, non-small cell lung cancer; PDL1, programmed cell death ligand 1; anti-PD-(L)1, anti-programmed cell death protein-1/ligand 1 inhibitors; PD, progressive disease; PFU, plaque forming units; PR, partial response; pts, participants; Q2W, biweekly; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TEAE, treatment-emergent adverse event

**DISCLOSURES:** This study was funded by Johnson & Johnson. Authors VMG, EC, LV, EF, RB, CM, EG-L, RV, JUS-C, SAP-P are study investigators receiving institutional support from Johnson & Johnson. AH, JB, JD, AC, DS, SW, SR, RJ, SB, RB are employees of Johnson & Johnson.

**REFERENCES**  
1. Ferruci et al. Cancers. 2021;13(6):1383.

**ACKNOWLEDGMENTS:** The authors thank SciVoc Consulting Inc., Toronto, Canada for providing editorial and design assistance for the poster.

Copies of this poster obtained through QR, AR and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.

