2025 ASCO® ANNUAL MEETING

Clinical responses to SYNC-T Therapy: In situ personalized cancer vaccination with intratumoral immunotherapy in patients with metastatic castration-resistant prostate cancer (mCRPC)

Charles J. Link, MD[1,2] , Stephen Kee, MD[1], George C Prendergast, PhD[2], Lucinda Tennant, MS[1], Renata Barco, MD[3], Mario Mautino, PhD[1], Gabriela R Rossi, PhD[1], Daniel K. Recinella, MBA[1], David J Vaughan, MD[1], Richard G Harris, MD[1,4], Eduardo Cortes[5], Ricky T. Tong, MD, PhD[2, 6], Jason R. Williams, MD[5] and Carlos A Vargas, MD[3] , (1)Syncromune, Inc., Fort Lauderdale, FL, (2)Lankenau Institute for Medical Research, Wynnewood, PA, (3)DioMed Hospital, Ciudad de México, EM, Mexico, (4)UroPartners, Westchester, IL, (5)Williams Cancer Institute, Beverly Hills, CA, (6)Main Line Health, Wynnewood, PA

Ricky T. Tong, M.D., Ph.D.

Lankenau Medical Center, part of Main Line HealthCare

Key Takeaways

1

SYNC-T immunotherapy includes partial oncolysis followed by intratumoral infusion of a multi-target drug to generate a systemic immune anti-tumor response

2

Efficacy demonstrated 87% ORR with 53% CR in subjects with advanced metastatic prostate cancer

3

SYNC-T therapy was well tolerated with mostly Grade 1 or 2 adverse events (95%) due to low dose and minimal systemic drug exposure

mCRPC Responds Poorly to Conventional Systemic Immunotherapy

- Prostate cancer is an immunologically “cold” tumor:
  - Low expression of PD-L1
  - Minimal T cell infiltration
  - Low tumor mutational burden
  - An immunosuppressive TME
- ORR to anti-PD-1 Abs are 3 - 5%[1] with **little to no overall survival benefit** [2-5]
  - Combination anti-PD-1 + anti-CTLA-4 show low ORRs of 0 - 25%[6,7]
  - **Significant rates of Grade 3 and 4 toxicity**, especially with checkpoint combinations[6,7]
    - 42 – 53% Grade 3-4 treatment-related adverse events (TRAEs)
    - 26 – 40% discontinuation due to TRAEs

Currently the ability to combine targeted biologics is limited because of systemic autoimmune side effects

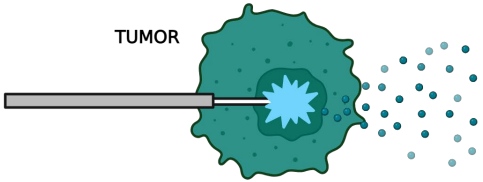
1. Antonarakis ES, et al. J Clin Oncol 38:395-405
2. Petrylak DP, et al., *JCO* **41**, 19-19(2023).DOI:10.1200/JCO.2023.41.6_suppl.19
3. Kwon ED, et al. Lancet Oncol. 2014 Jun;15(7):700-12. doi: 10.1016/S1470-2045(14)70189-5.
4. Powles T., et al. Nat Med. 2022 January; 28(1):144-153. doi:10.1038/s41591-021-01600-6.
5. Graff JN, et al. Future Oncol. 2021 Aug;17(23):3017-3026. doi: 10.2217/fon-2020-1008.
6. Sharma P., et al. Cancer Cell. 2020 Oct 12;38(4):489-499.e3. doi: 10.1016/j.ccell.2020.08.007..
7. Shenderov E, et al. Prostate. 2021 May;81(6):326-338. doi: 10.1002/pros.24110.

SYNC-T Therapy Concepts

- Designed to provide **personalized** ***in situ*** cancer therapy through partial oncolysis of the subject's tumor to enhance immune activation
- Utilizes antigen release and the multi-target drug approach to both **reduce immune suppression and enhance immune activation**
- The immune therapy is designed to generate a **systemic anti-tumor T cell response**
- Intratumoral targeting allows for low dose administration and high loco-regional concentrations with **minimal systemic exposure that results in reduced toxicity**

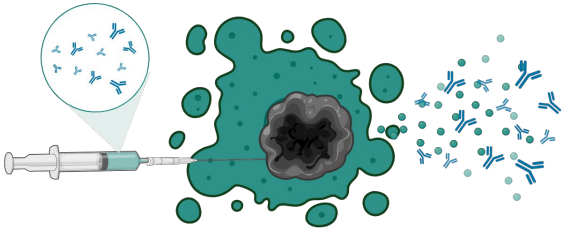
SYNC-T® Personalized *In Situ* Therapy

A PORTION OF THE TUMOR IS LYSED USING TARGETED FREEZING



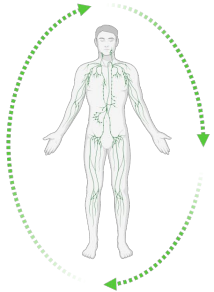
Tumor Antigens & DAMPs release

SV-102 BIOLOGIC INFUSED INTO LYTIC ZONE



Multi-targeted immune activation within the TME and regional lymph nodes leads to T cell activation and proliferation

SYSTEMIC ANTI-TUMOR RESPONSE



Tumor-specific T cells migrate and attack tumors systemically

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Figure created using BioRender

SYNC-T Drug Candidate SV-102: Multi-Target Drug with 4 Active Immunotherapeutic Ingredients

SV-102

Anti-CTLA-4 mAb
enhances anti-tumor responses by blocking CTLA4, stimulating T cell priming, and downregulating Treg-mediated suppression

Anti-PD-1 mAb
blocks PD1-mediated T cell exhaustion, rescuing T cell cytotoxic activity

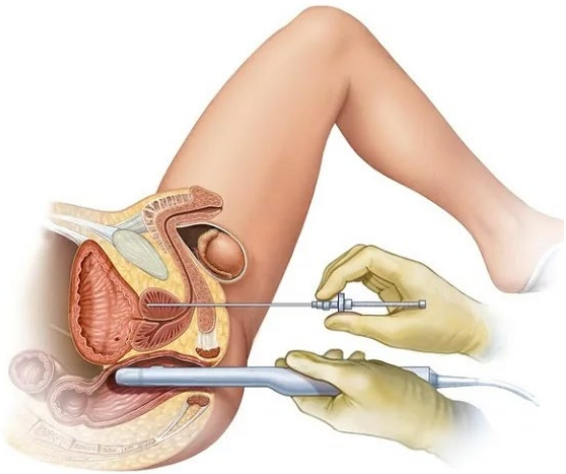
CD40 agonist mAb
activates antigen-presenting cells (APCs)

TLR9 agonist
enhances Th1-mediated anti-tumor responses and stimulates plasmacytoid dendritic cells and APCs in the tumor draining lymph nodes

SYNC-T Therapy Procedure for mCRPC

SYNC-T Therapy uses clinical procedural skills that are routine for Urologists:

- Procedure employs commonly used MR and/or transrectal ultrasound (TRUS) for probe placement in the prostate
- Oncolysis is first performed via targeted freezing using the ICESPHERE™ Cryoablation Needle to generate ~ 10 mm ice ball, followed by passive thawing
- After passive thawing, 15 ml of the SV-102 multi-target biologic is infused into the lytic zone at a rate of 3 ml/min
- For soft tissue metastases outside of the prostate that are targeted for oncolysis, the procedure is performed by Interventional Radiologists using CT or US-guided percutaneous needle placement



TRUS-Guided Transperineal Approach for Prostate Tumors

SYNC-T with SV-102 Phase 1 Trial Inclusion & Exclusion Criteria

Investigator-Initiated Trial evaluating safety and efficacy of SYNC-T Therapy SV-102 for mCRPC

Open label, single arm study

KEY INCLUSION CRITERIA

- Histologically confirmed metastatic prostate cancer
- Failure of previous treatment with one or more approved second-generation androgen-receptor-pathway inhibitors with or without prior chemotherapy or refused hormone therapy
- Measurable disease by RECIST 1.1 criteria
- Soft-tissue disease that can be targeted by SYNC-T Therapy
- Ability to provide informed consent

KEY EXCLUSION CRITERIA

- Known other primary malignancy other than prostate cancer that is progressing or has required active treatment in previous 3 years
- Obstructed urinary system before or after stenting
- Undergone major surgery or local prostate intervention within 28 days prior to first SYNC-T cycle
- Active infection requiring systemic therapy
- Received a live vaccine within 30 days prior to enrollment
- Significant cardiac or other medical illness

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SYNC-T with SV-102 Phase 1 Trial Design & Endpoints

TRIAL DESIGN

- Up to 12 cycles of SYNC-T SV-102 at 4-week intervals to achieve best response
- Oncolysis combined with SV-102 fixed dose of 15 mL volume
- Baseline imaging of bone scan and/or PET/CT, and MRI of prostate
- Response assessment every 8 weeks
- Durability of response measured every 12 weeks after completion of therapy

ENDPOINTS

PRIMARY

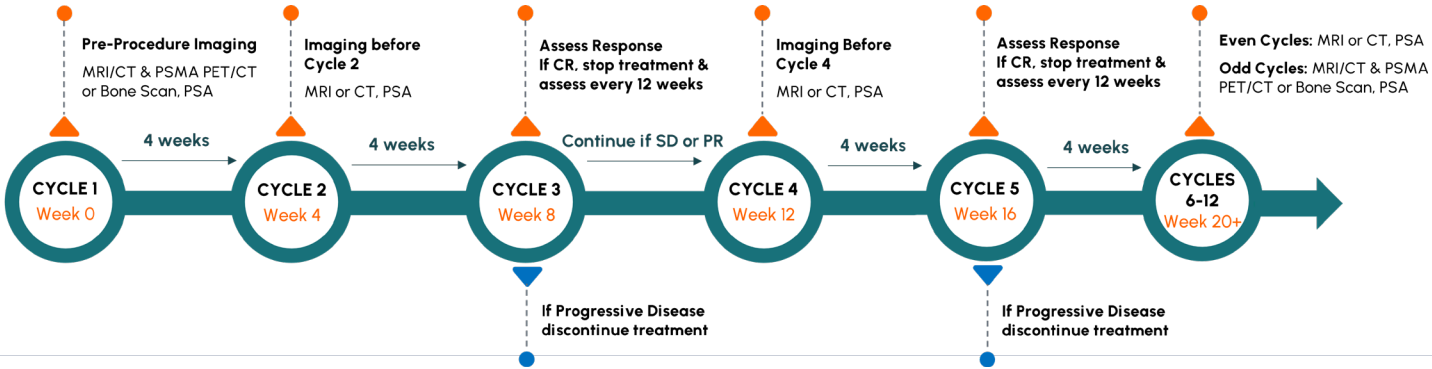
- Evaluate safety & toxicity

SECONDARY

- ORR by RECIST 1.1
- rPFS by PCWG3
- OS

EXPLORATORY

- Assess pharmacokinetics and immunogenicity of each SV-102 API
- Exploratory biomarker analysis



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Subject Characteristics

- 15 subjects enrolled and evaluable with data cutoff of May 1, 2025

Baseline Characteristics		n = 15
Demographics	White	9 (60%)
	Hispanic	5 (33%)
	Black	1 (7%)
Age	Median: 61 (Range: 49-74)	
ECOG	PS-0	7 (47%)
	PS-1	7 (47%)
	PS-2	1 (6%)
Bone Mets		13 (87%)

Prior Therapy

Prior Therapy	(n = 15)
ADT and/or 2nd generation anti-androgen or subject refused	**15** (100%)
Chemotherapy	**3** (20%)
Radiation Therapy	**5** (33%)
Immunotherapy	**2** (13%)

SYNC-T Therapy SV-102 Response Summary

Subject	# Cycles	Best Response
SV-102-01	3	Partial Response
SV-102-02	2	Complete Response
SV-102-03	12	Complete Response
SV-102-04	9	Complete Response
SV-102-05	2	Complete Response
SV-102-06	6	Partial Response
SV-102-07	5	Partial Response
SV-102-08	2	Stable Disease
SV-102-09	8	Complete Response
SV-102-10	9	Partial Response
SV-102-11	9	Complete Response
SV-102-12	14*	Partial Response
SV-102-13	10	Complete Response
SV-102-14	5	Stable Disease
SV-102-15	3	Complete Response

*Received Ethics Committee approval to give additional treatment

Best Response in Evaluable Subjects (n=15)*	
Disease Control Rate	**15 (100%)**
Complete Response*	**8 (53%)**
Partial Response*	5 (33%)
Stable Disease	2 (13%)
Progressive Disease	0 (0%)
Overall Response Rate	**13 (87%)**

- **PSA results:**
  - Seven subjects (47%) declined by > 50% or had PSA < 0.02 throughout treatment (n=2)
  - One subject (7%) declined by > 40%
- **3 subjects have died off study**

***Independent radiological review completed on 5/24/2025 reported ORR of 87%, CR of 40% and PR of 47%**

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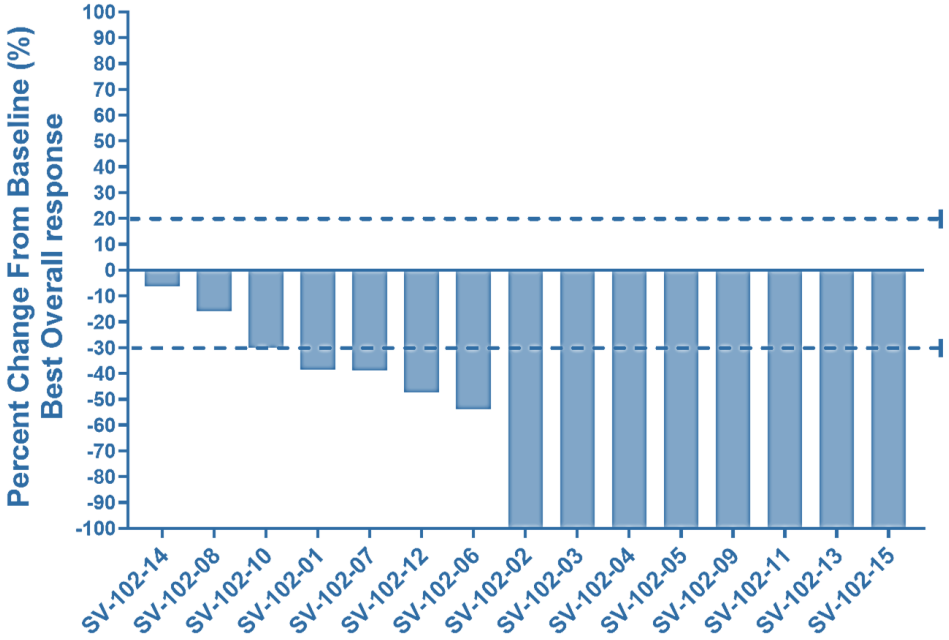
NCT05544227 – Data presented as of May 1, 2025; all subjects enrolled by Jan 10, 2024. Total N = 15 subjects

RECIST 1.1 Assessment



- Complete response (CR) occurred in 8 subjects (53%, the two-sided 95% Confidence interval (CI), 29 to 79)
- Complete resolution of primary, bone, and soft tissue metastases

Summary of Key Results

17.2 Months Median Follow-Up

Results In Months (n=15)	
Median Time to Response (range)	**2.9** (1.8–4.8)
Median Duration of Response (range)	**12.1** (1.1–22.4)
Median rPFS (range)	**14.2** (4.8–24.1)
Median OS (range)	**Not Reached** (6.1–24.6)

- Among the 15 subjects, 3 have died resulting in 80% survival with a 17.2 month median follow-up

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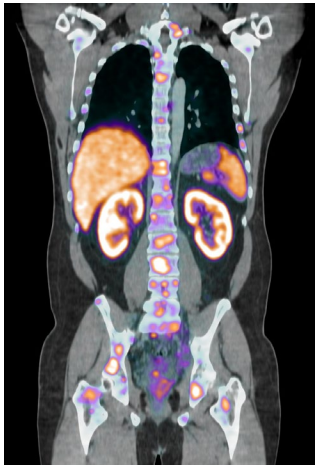
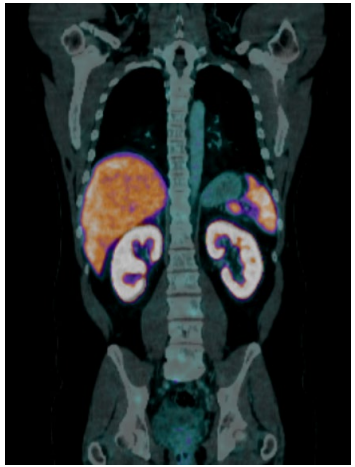
Subject SV-102-09: Complete Response

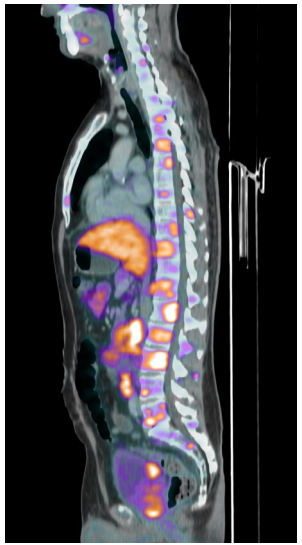
- Tumor was PD-1/ PD-L1 NEG and proficient MMR
- Complete resolution of > 50 bone metastases
- rPFS = 19.5+ months
- OS = 20.5+ months



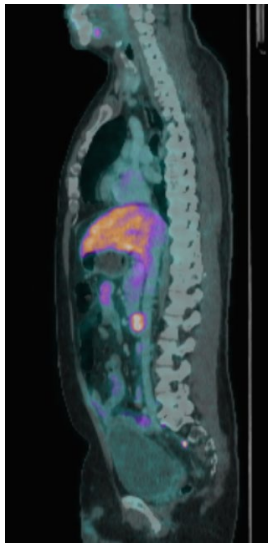
PRE-THERAPY. May 2023 coronal PSMA PET/CT shows extensive bone metastases (greater than 50)



POST-THERAPY. December 2023 coronal PSMA PET/CT shows complete resolution of all bone metastases



PRE-THERAPY. May 2023 sagittal PSMA PET/CT shows extensive bone metastases

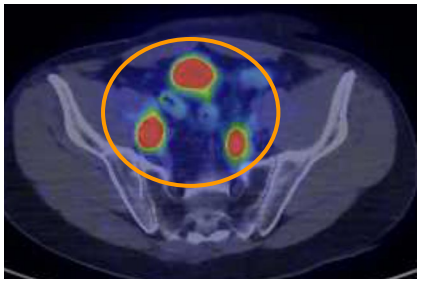


POST-THERAPY. December 2023 sagittal PSMA PET/CT shows complete resolution of all bone metastases

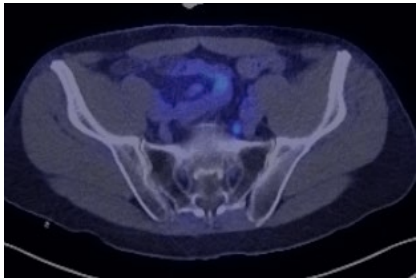
Complete resolution of > 50 bone metastases after 7 treatment cycles

Subject SV-102-04: Complete Response

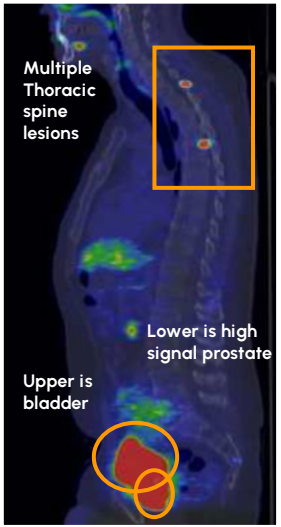
- After Cycle 4, subject was confirmed via RECIST 1.1 as a Complete Response with resolution of bone metastases, lymph node metastases and prostate tumor
- rPFS = 14.2 months
- OS = 24.6+ months



PRE-THERAPY. 3/2023 axial view shows a markedly abnormal PSMA PET/CT, high SUV in prostate, pelvic lymph nodes, and spine



POST-THERAPY. 9/2023 axial PSMA PET/CT showing minimal signal uptake in posterior aspect on T4



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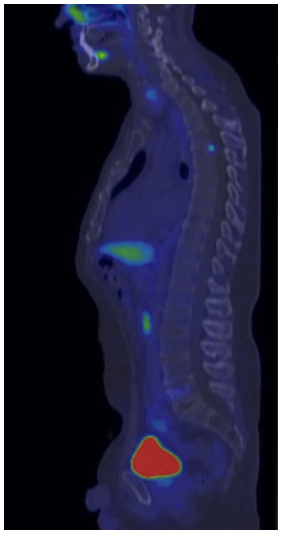
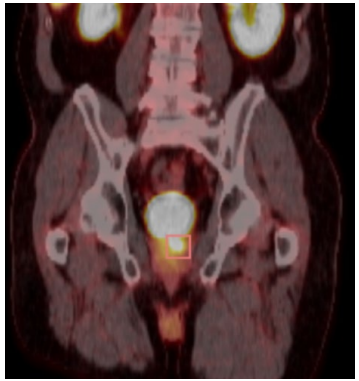


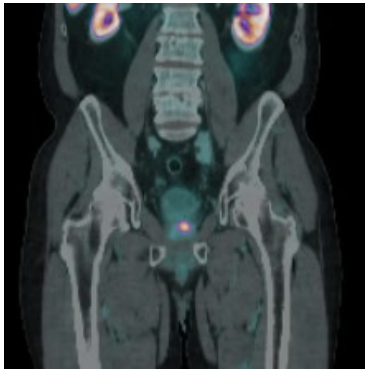
POST-THERAPY. 9/2023 sagittal PSMA PET/CT showing resolution of disease

Subject SV-102-03: Complete Response

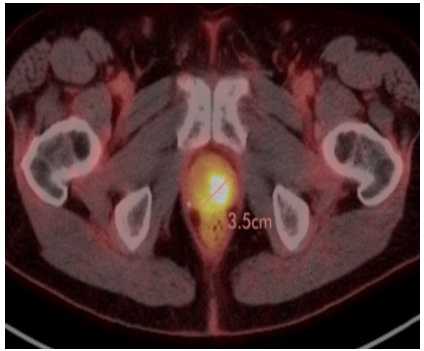
- Subject had persistent high-signal area on diffusion-weighted MR images within the prostate
- Biopsy of that area was negative, confirming complete response which remains durable
- rPFS = 24.1+ months
- OS = 24.4+ months



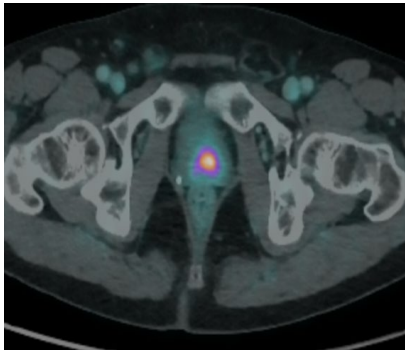
PRE-THERAPY. 2/2023: PSMA PET/CT coronal scan at baseline shows extensive involvement in prostate and in left 10th rib



POST-THERAPY. Follow-up PSMA PET/CT from 10/2023 coronal image showing resolution of bone lesion and significant reduction in prostatic disease



PRE-THERAPY. 2/2023: PSMA PET/CT axial scan at baseline shows prominent 3.5 cm lesion in both lobes of the prostate, appearing to involve the capsule



POST-THERAPY. Follow-up PSMA PET/CT from 10/2023 coronal image showing resolution of bone lesion and significant reduction in prostatic disease

Safety & Tolerability

SYNC-T demonstrated ability to target multiple mechanisms while avoiding systemic autoimmune side effects

- 41 Treatment Emergent Adverse Events (TEAEs) were observed in 13 subjects
- Majority (95%) TEAEs were Grade 1 or 2
- Most common TEAEs were fever and hematuria
- Only two Grade 2 immune-related adverse events (hypothyroidism and hepatitis)
- Two Grade 3 TEAEs (voiding problem and spinal cord compression)
- No Grade 4 or 5 TEAEs

	All TEAEs N (%) Events	Grade 1+2 TEAEs	Grade 3 TEAEs	Grade 4/5 TEAEs
Blood and Lymphatic System Disorder				
Anemia	1 (6.7) 1	1 (6.7) 1	0	0
Cardiac Disorders				
Chest Pain	1 (6.7) 1	1 (6.7) 1	0	0
Ear and Labyrinth Disorders				
Vertigo	1 (6.7) 1	1 (6.7) 1	0	0
Endocrine Disorders				
Hypothyroidism	1 (6.7) 1	1 (6.7) 1	0	0
Polydipsia	1 (6.7) 1	1 (6.7) 1	0	0
Gastrointestinal Disorders				
Diarrhea	2 (13.3) 2	2 (13.3) 2	0	0
Rectal Discomfort	1 (6.7) 1	1 (6.7) 1	0	0
Vomiting	2 (13.3) 2	2 (13.3) 2	0	0
General Disorders & Administration Site Conditions				
Fever	3 (20.0) 4	3 (20.0) 4	0	0
Fatigue	1 (6.7) 2	1 (6.7) 2	0	0
Infections and Infestations				
COVID-19	1 (6.7) 1	1 (6.7) 1	0	0
Injury, Poisoning and Procedural Complications				
Right Shoulder Fracture	1 (6.7) 1	1 (6.7) 1	0	0
Investigations				
Hepatic Enzymes Increased	1 (6.7) 1	1 (6.7) 1	0	0
Musculoskeletal and Connective Tissue Disorders				
Low back pain	1 (6.7) 1	1 (6.7) 1	0	0
Myalgias	1 (6.7) 2	1 (6.7) 2	0	0
Neoplasms benign, Malignant and Unspecified				
Skin Squamous Cell Carcinoma	1 (6.7) 1	1 (6.7) 1	0	0
Nervous System Disorders				
Spinal Cord Compression	1 (6.7) 1	0	1 (6.7) 1	0
Renal and Urinary Disorders				
Hematuria	4 (26.7) 4	4 (26.7) 4	0	0
Urethral Discomfort	1 (6.7) 1	1 (6.7) 1	0	0
Urinary Hesitancy	1 (6.7) 1	1 (6.7) 1	0	0
Urinary Retention	2 (13.3) 4	1 (6.7) 3	1 (6.7) 1	0
Urinary Tract Infection	2 (13.3) 2	2 (13.3) 2	0	0
Skin and Subcutaneous Tissue Disorders				
Diaphoresis / hyperhidrosis	2 (13.3) 2	2 (13.3) 2	0	0
Rash	2 (13.3) 2	2 (13.3) 2	0	0
Vascular Disorders				
Perineal Hematoma	1 (6.7) 1	1 (6.7) 1	0	0

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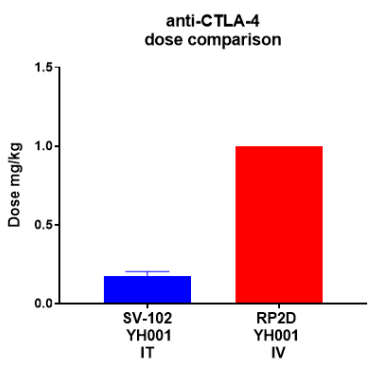
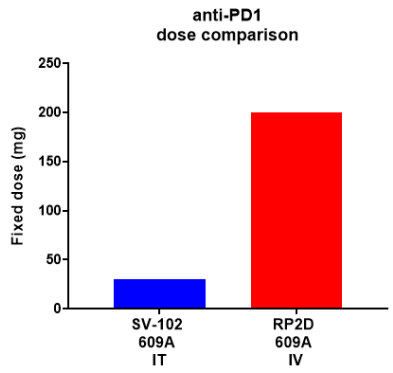
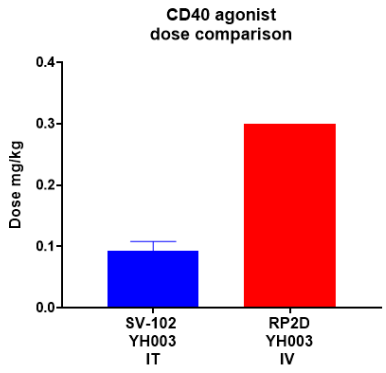
Dose & Exposure of SV-102 With Individual Components

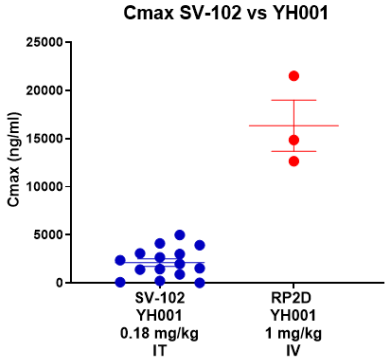
APIs in SV-102 are dosed at much lower levels than IV RP2D

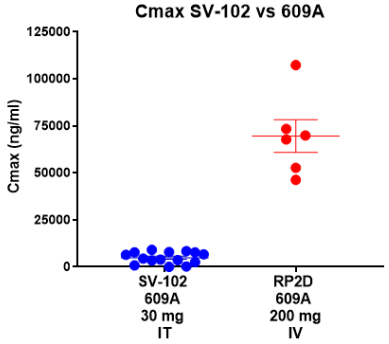
Much lower systemic exposure is observed

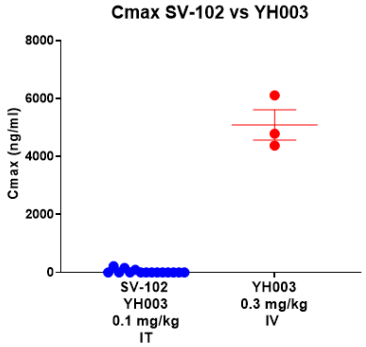












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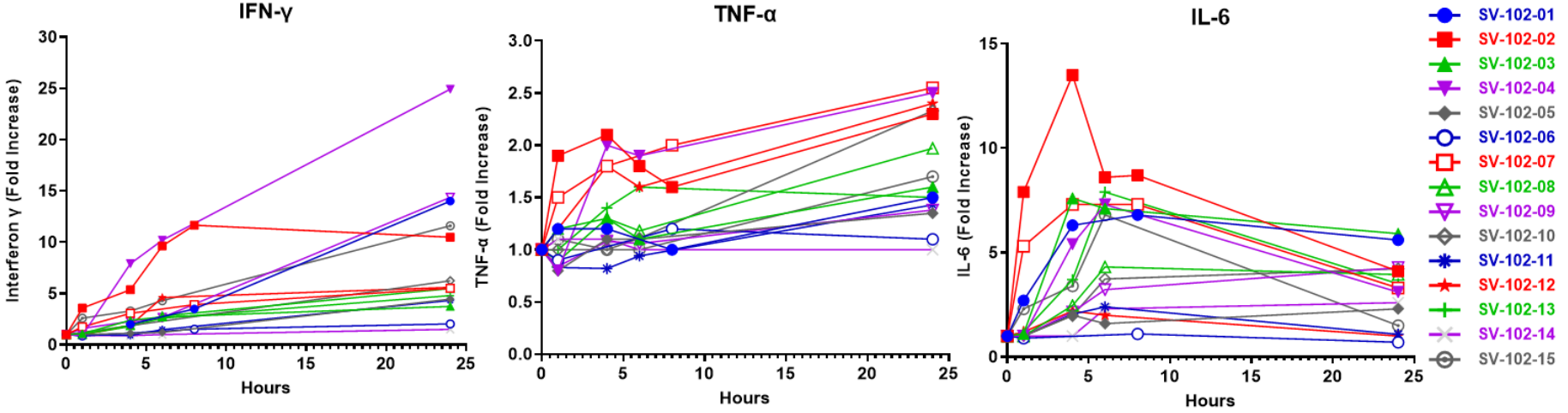
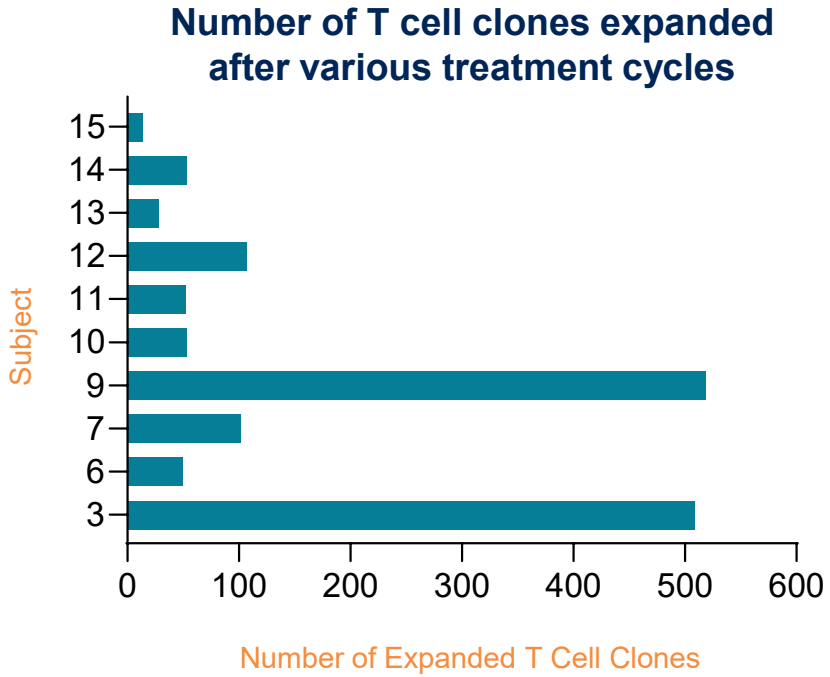
Anti-Tumor Cytokines Are Rapidly Induced by SYNC-T Therapy



- Pro-inflammatory cytokines increase during the first 24 hours after SYNC-T Therapy
- IFNγ, TNFα and IL-6 all show significant increases from pre-treatment

Remarkable Increase in Frequency of New T Cell Clones

- SYNC-T therapy induced a robust peripheral polyclonal T cell expansion, which increases after additional treatment cycles
- Data shows expanded TCRß clones associated with known MHC-restricted tumor antigens
- SYNC-T therapy may drive a positive selection of polyclonal responses against some tumor antigens



Trial Limitations

- Small number of subjects treated thus far with SYNC-T Therapy SV-102
- Single-center
- Heterogeneous population with both hormone-refractory (10) and hormone-naive subjects (5)

Key Takeaways

1

SYNC-T immunotherapy includes partial oncolysis followed by intratumoral infusion of a multi-target drug to generate a systemic anti-tumor immune response

2

Efficacy demonstrated 87% ORR with 53% CR in subjects with advanced metastatic prostate cancer

3

SYNC-T therapy was well tolerated with mostly Grade 1 or 2 adverse events (95%) due to low dose and minimal systemic drug exposure

Summary

- SYNC-T Therapy SV-102 for mCRPC demonstrates highly encouraging clinical activity
- A significant portion of subjects in this pilot study have achieved either a complete response or near complete response with resolution of all bone metastases
- Initial safety data demonstrated no Grade 3 or 4 autoimmune adverse events
- The infusion of SYNC-T Therapy SV-102 directly into the tumor uses significantly lower doses than delivering immunotherapies systemically via an IV
- **Current status: Multi-center U.S. Phase 2a trial is underway (LEGION-100 trial)**

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Adjunct Professor
Syncromune Executive Chairman

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Jason Williams, M.D.
Director, Interventional Oncology

Renata Barco, M.D.

Carlos Vargas, M.D.
Interventional Oncologist

Eduardo Cortes

Syncromune, Inc.

Gerald Andriole, M.D.
Chief Medical Officer, Urology

David Vaughan, M.D.
EVP, Medical Affairs

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EVP, Immunology

Richard Harris, M.D.
EVP, Medical Operations

Stephen Kee, M.D.
EVP, Clinical Operations

Mario Mautino, Ph.D.
Chief Scientific Officer

Lucinda Tennant
EVP, Head of Clinical Operations

Dan Recinella
EVP, Medical Device Development

Summary Slide for Non-Clinicians

- SYNC-T Therapy SV-102 was studied in 15 subjects with metastatic prostate cancer
- The therapy involves breaking down part of the tumor with a needle, followed immediately by the infusion of a drug through the same needle
- All subjects had either some shrinkage or the tumor stopped growing for a period of time
- Over half the subjects had their cancer go into complete remission
- Subjects experienced mild side effects from the therapy
- The treatment is now being studied in men with recurrent prostate cancer in a larger study called the LEGION-100