RubiusTherapeutics

REALIZING THE POWER OF RED™
A NEW ERA IN CELLULAR MEDICINE

JUNE 2022

Forward-Looking Statements

This presentation may contain forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our clinical results and other future conditions. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial or business performance, conditions, plans, prospects, trends or strategies and other financial and business matters; our current and prospective product candidates; current or planned clinical trials and preclinical activities, including timing related to such trials and activities and expected results; research and development costs; current and prospective collaborations; the estimated size of the market for our product candidates; the timing and success of our development and commercialization of our anticipated product candidates; and the availability of alternative therapies for our target market are forward looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, investors are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Rubius recommends that investors independently evaluate specific investments and strategies. For further information regarding these risks, uncertainties and other factors, you should read the “Risk Factors” section of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, our Annual Report on Form 10-K filed for the period ended December 31, 2021 and subsequent filings with the Securities and Exchange Committee.

This presentation may contain tradenames, trademarks or servicemarks of other companies. Rubius does not intend the use or display of other parties’ tradenames, trademarks or servicemarks to imply a relationship with, or endorsement or sponsorship of, these other parties.

Strong Execution of Key Priorities

PROGRAMMABLE PLATFORM ENABLES MULTIPLE MODALITIES TO TARGET IMMUNE PATHWAYS

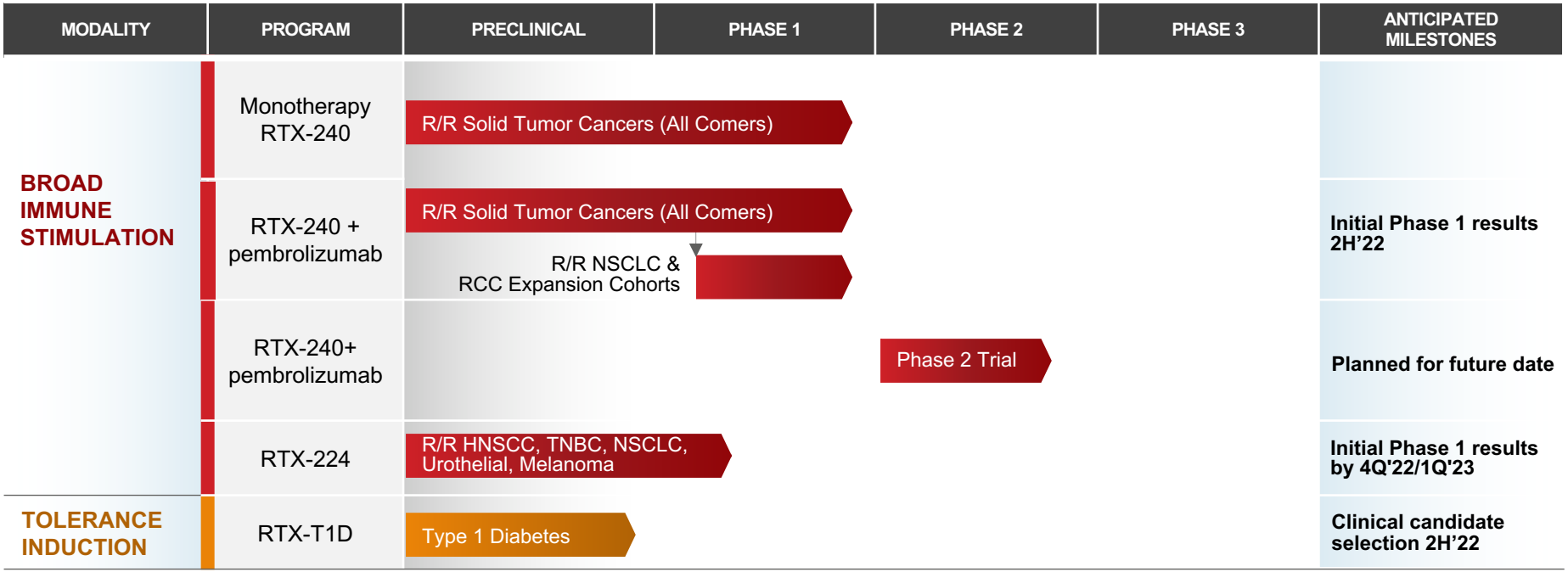
- **Presented updated clinical data*** from monotherapy Phase 1 arm of RTX-240 in advanced solid tumors clinical trial, showing clinical responses with favorable tolerability in PD-(L)1 refractory disease
- **Advanced enrollment** in Phase 1 arm of RTX-240 + pembrolizumab in advanced solid tumors; expanded to focus on NSCLC and RCC patients
- **Dosing patients** in Phase 1/2 clinical trial of RTX-224; initial results expected 4Q'22/1Q'23
- **Presented preclinical proof of concept** for immune tolerance induction in Type 1 Diabetes
- **Successfully scaled to 200L bioreactors** and providing uninterrupted clinical supply for ongoing oncology studies

The Boston Globe TOP PLACES TO WORK 2021

PBN PROVIDENCE BUSINESS NEWS BEST PLACES WORK AWARDS Winner 2021

*Clinical data from 34 patients for safety and 27 for efficacy analysis at the time of the cut-off March 4, 2022

Anticipated Milestones from Rubius' Broad Wholly Owned Pipeline



Expanded ongoing Phase 1 arm of RTX-240 + pembrolizumab to focus on NSCLC and RCC patients to inform Phase 2 clinical trial

NSCLC = Non-small cell lung cancer; NHSCC = Head and neck squamous cell carcinoma; RCC = Renal cell carcinoma; TNBC = Triple negative breast cancer

Rubius Therapeutics

RUBIUS RED PLATFORM®

The Promise of Red Cell Therapeutics™: The Future of Cellular Therapy

POTENTIALLY TRANSFORMATIVE
ALLOGENEIC CELLULAR THERAPY CANDIDATES DESIGNED TO BE…

POTENT

Modular platform that mimics immune biology

Cellular presentation of potent immune modulators

TOLERABLE

Biodistribution confined to vasculature and spleen

Broadens therapeutic window in cancer

Avoids immunosuppression in autoimmunity

SCALABLE

Off-the-shelf cellular therapy candidate from Rubius manufacturing site

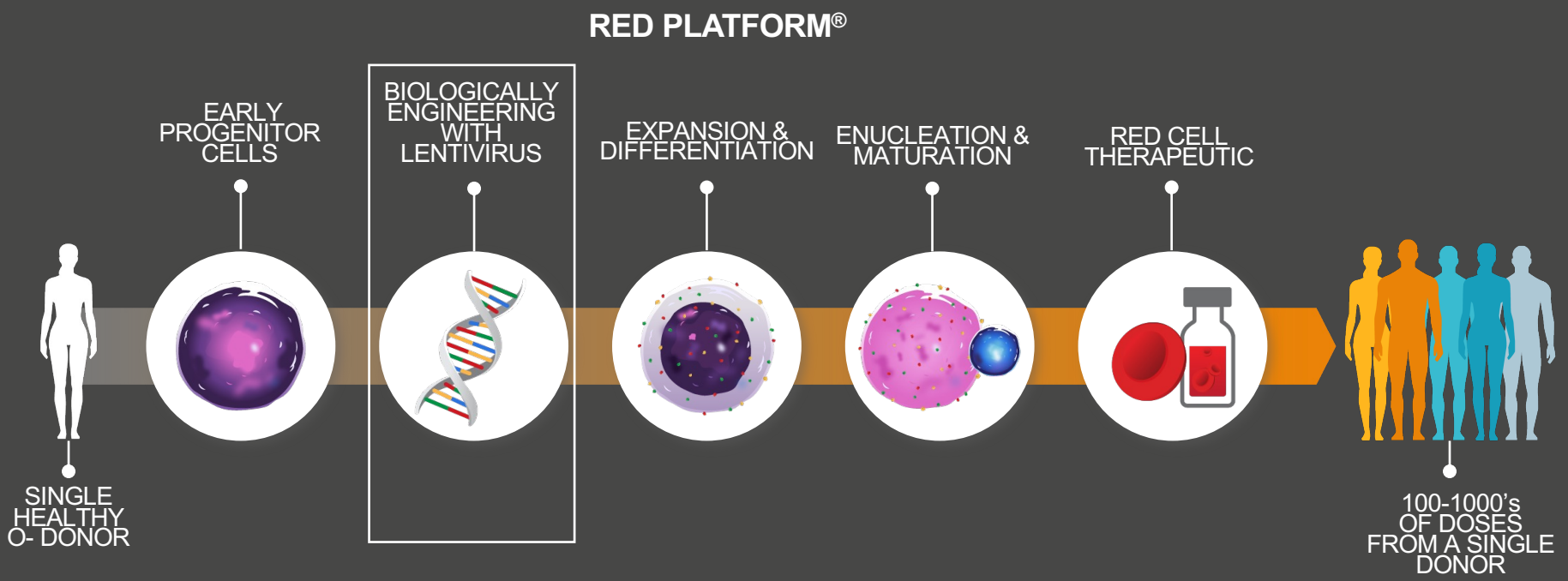
CONVENIENT

Administered in clinic vs. cell therapy lab

Outpatient

No required lymphodepletion

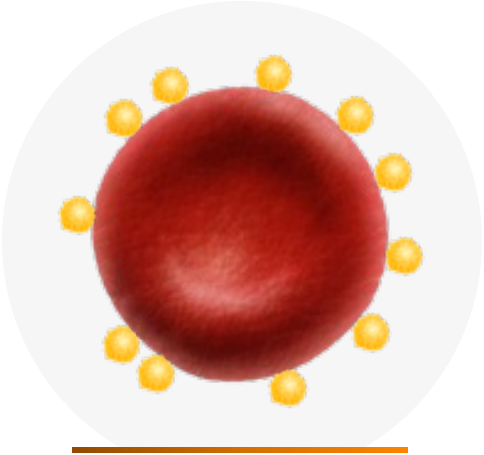
Highly Versatile and Programmable Platform: More Than 1,000 Proteins Engineered Since Platform Inception



- The only modification from one product candidate to the next is the gene cassette in the lentiviral vector
- Platform leverages common processes and infrastructure

Ability to Express Therapeutic Proteins Anywhere on or Within the Cell

RCTs with proteins or peptides expressed inside the cell are phagocytized (ingested) by dendritic cells or macrophages, inducing tolerance to those proteins



Proteins expressed on the outside of the RCT can be used to activate or inhibit immune cells via binding to receptors on those cells

These two combined modalities enable antigen-specific immune activation in cancer or tolerance in autoimmunity

- Platform versatility enables targeting of multiple immune pathways to treat a range of diseases
- Hundreds of thousands of copies of expressed therapeutic proteins per cell provide potent biologic effects

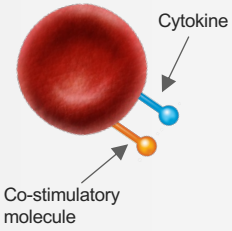
The RED PLATFORM Enables Multiple Modalities in Cancer, Autoimmune Diseases and Beyond

MODALITIES TODAY

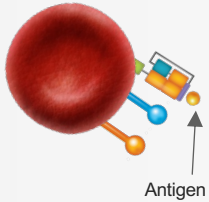
FUTURE OF RCTS

ONCOLOGY

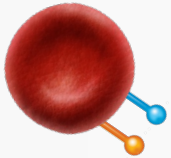
Induce broad immune stimulation



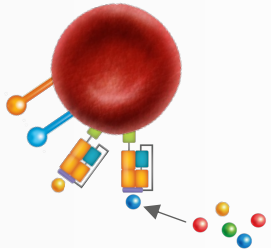
Antigen-specific immune stimulation to drive tumor-specific responses



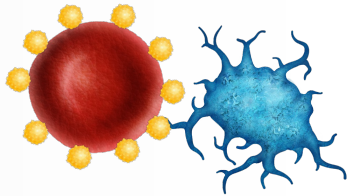
Broad immune stimulation with additional payloads and proteins for enhanced potency



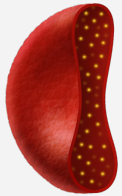
Loadable MHC to express multiple antigens on the same cell



Dendritic cell activation with or without an antigen

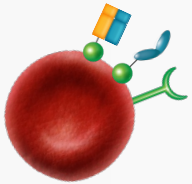


AUTOIMMUNE

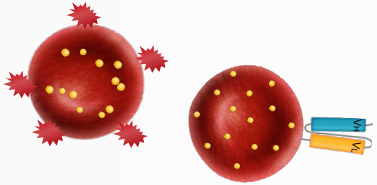


Target antigen-presenting cells to create T cell tolerance to specific antigens

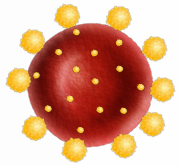
Target T cells directly to create antigen-specific tolerance



Arm RCTs with undisclosed immunomodulators or targeting moieties to induce tolerance



Prevent immunogenicity to enzyme replacement and gene therapy



Potential to Realize Broad Depth of Value of Red Cell Therapeutics

FOUNDATIONAL
INTELLECTUAL PROPERTY COVERING:

- Pioneering processes for engineering and culturing RCT product candidates
- Issued U.S. patents cover RTX-240, RTX-321 and RTX-224
- Cover composition of matter, method of treating and method of making

RAPIDLY EXPANDING PATENT PORTFOLIO

15
Issued and Allowed U.S. Patents

29
Patent Families

>170
Applications Pending Worldwide

2039
Earliest Patent Expiration*

*Does not consider patent term adjustments or extensions

RubiusTherapeutics

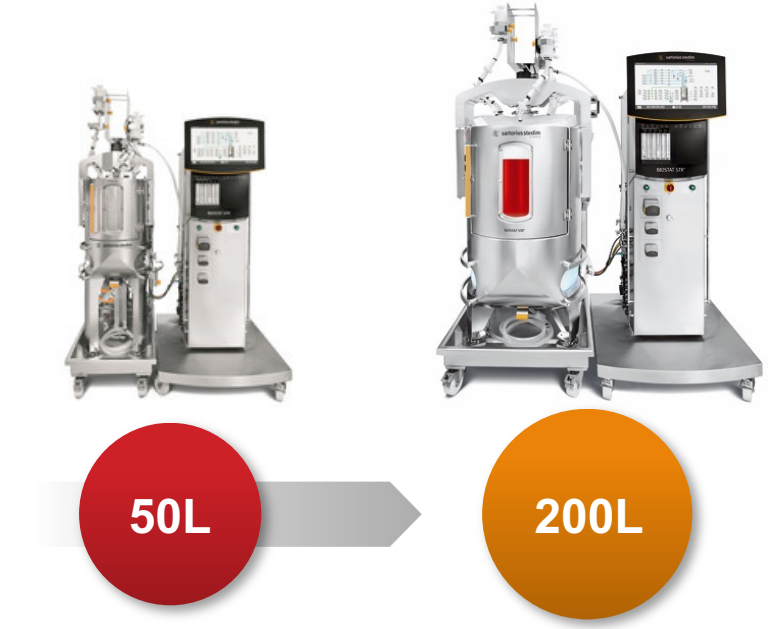
ADVANCES IN MANUFACTURING

Rubius Fully Owned Manufacturing and Integrated Technical Development & Operations

- Small-scale production, process development, cGMP manufacturing, analytical development & quality operations
- Providing cGMP clinical supply for RTX-240 and RTX-224 trials
- Highly experienced cell therapy technical operations team with scalable process
- Significant potential to expand manufacturing capabilities based on future needs

Recent Manufacturing Achievements

SUCCESSFULLY SCALED FROM 50L TO 200L FOR RTX-240



ADDITIONAL ACCOMPLISHMENTS

- High success rate: **>90% lot success rate*** for RTX-240 clinical supply in 50L bioreactors
- **>200 doses administered** across 3 arms of RTX-240 Phase 1 and RTX-224 Phase 1 trials
- High transduction efficiency: **>90% of cells are transduced** with therapeutic proteins
- **Highly consistent protein expression**

Scale-up to support potential pivotal trial & commercialization of RTX-240

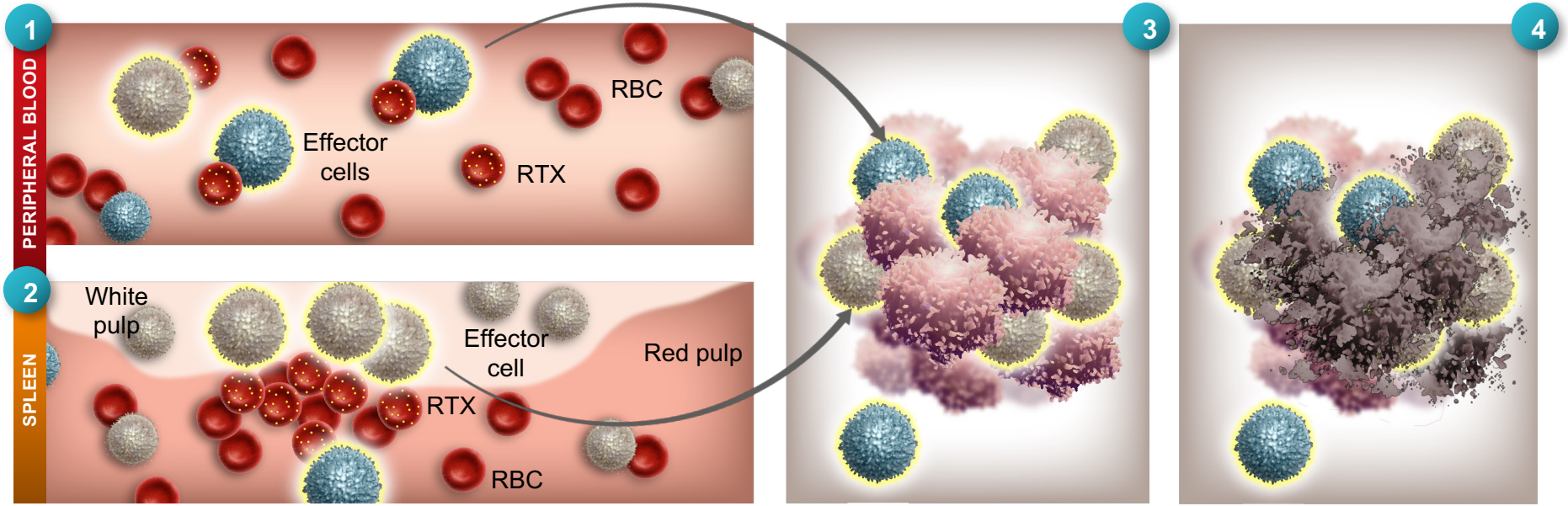
*Defined as from batch start to released drug product

Rubius Therapeutics

SOLVING THE CHALLENGES OF IMMUNE AGONISTS IN ONCOLOGY

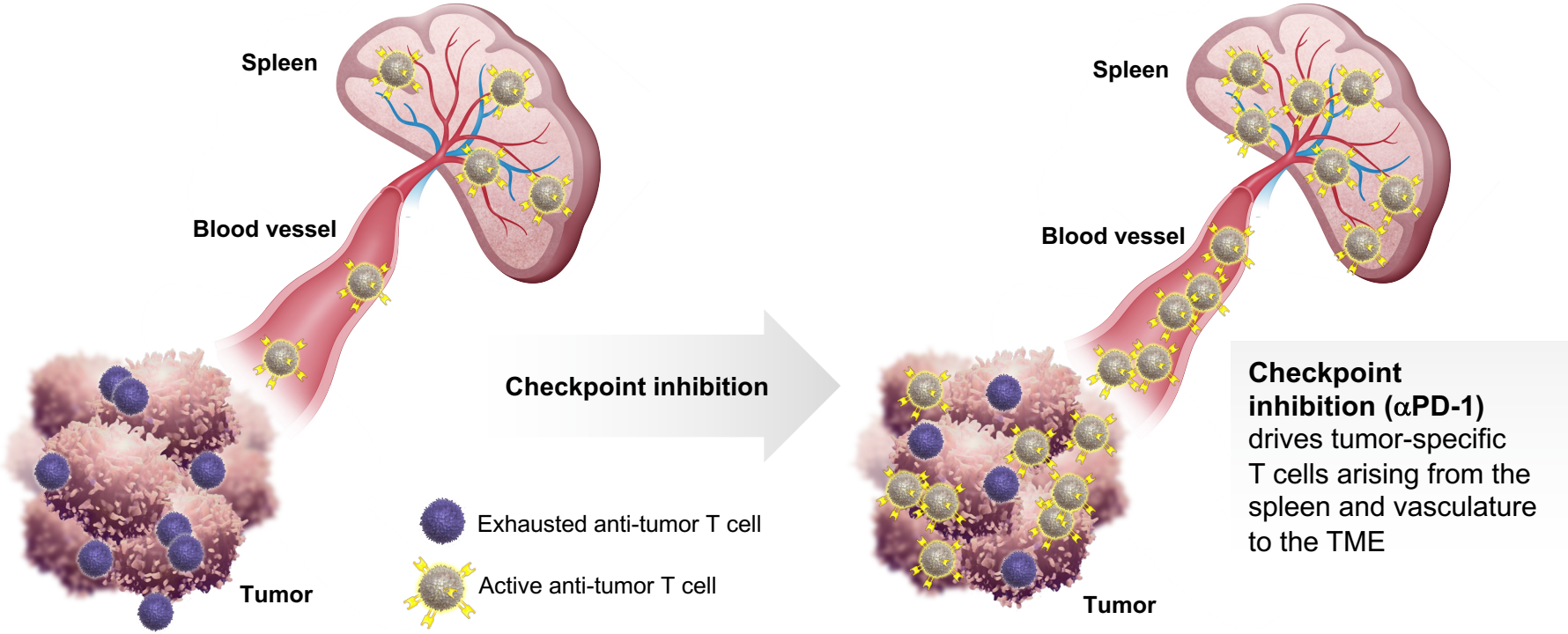
Proposed Mechanism of Action of Oncology RCTs

1 ACTIVATION | 2 EXPANSION | 3 TRAFFICKING | 4 TUMOR KILLING



Potential for enhanced efficacy and safety versus agonists antibodies and recombinant cytokines by confining RCTs to the vasculature and spleen

Tumor-Specific T Cells Coexist with Red Blood Cells in the Spleen and Peripheral Blood



Checkpoint inhibition (αPD-1) drives tumor-specific T cells arising from the spleen and vasculature to the TME

PD-1 inhibitors and RCTs act on anti-tumor T cells outside of the tumor microenvironment; Activated cells traffic to the tumor

Wu, TD, et al. Grogan JL. Peripheral T Cell Expansion Predicts Tumour Infiltration and Clinical Response. Nature 2020
Beltra JC, et al. Wherry J. Developmental Relationships of Four Exhausted CD8+ T cell Subsets Reveals Underlying Transcriptional and Epigenetic Landscape Control Mechanisms. Immunity 2020

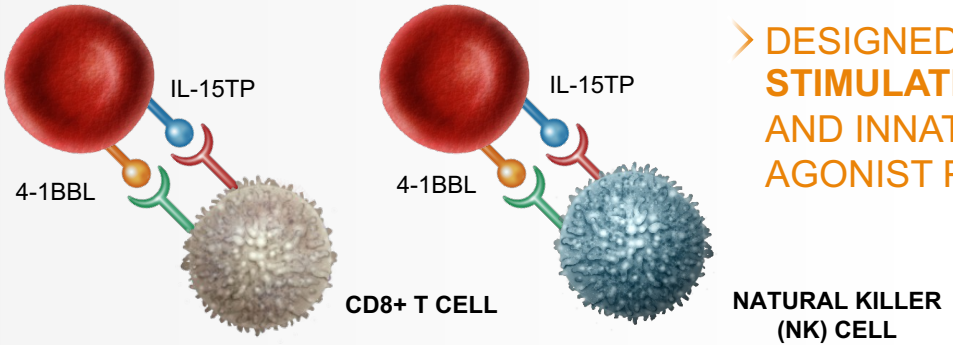
RubiusTherapeutics

RTX-240: BROAD IMMUNE STIMULATION

RTX-240 is Designed to Deliver Two Key Agonist Signals to the Immune System

BROAD IMMUNE SYSTEM STIMULATION

RTX-240 | (4-1BBL + IL-15TP)



DESIGNED TO **STIMULATE** ADAPTIVE AND INNATE IMMUNE CELL AGONIST PATHWAYS

POTENTIAL BENEFITS:

- Activate existing agonist pathways leading to enhanced potency
- Overcome resistance to immunotherapy
- Reduce toxicity given biodistribution confined to vasculature and spleen, widening the therapeutic window of agonists

Clinical Responses and Favorable Tolerability Results Observed in Patients with Solid Tumors Exposed to Prior PD-1/PD-L1 Therapy*

- 10 patients with advanced/refractory solid tumors had disease control (stable disease [SD]≥12 weeks, partial response [PR], unconfirmed [u]PR), including:
  - 3 PRs (1 PR, 2 uPRs) in certain patients with non-small cell lung cancer, anal cancer and uveal melanoma
  - 7 patients with SD≥12 weeks
    - 5 patients treated across the dose cohorts of 3e10 cells had SD, including
      - 4 patients with stable disease ≥6 months (2 NSCLC and 2 RCC patients)
- Statistically significant dose response in NK cell expansion (max fold change in number of circulating CD16/56+NK cells)
- Generally well tolerated across dose levels–no Grade 3/4 adverse events and no dose-limiting toxicities
- 5e10 Q3W selected as the recommended monotherapy Phase 2 dose
- Development next steps
  - Based on these data, expanding ongoing Phase 1 arm of RTX-240 + pembrolizumab to focus on RCC and NSCLC
    - Informing future Phase 2 combination trial of RTX-240 + pembrolizumab

RESULTS PROVIDE CLINICAL SUPPORT FOR THE RED PLATFORM
Unlocking Potential Across Oncology Given Programmable Nature of Platform

Safety population: n=34; Efficacy population: n=27; *Data cut-off: March 4, 2022

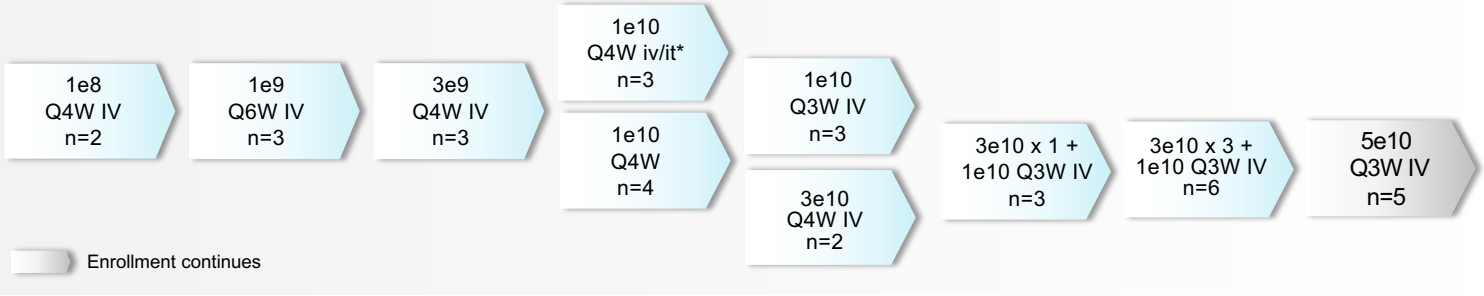
RubiusTherapeutics

UPDATED MONOTHERAPY RTX-240 PHASE 1 CLINICAL DATA IN ADVANCED SOLID TUMORS*

*Data cut-off March 4, 2022

Design of RTX-240 Monotherapy Phase 1 Arm in Advanced Solid Tumors

MONOTHERAPY
Relapsed/Refractory (R/R) or locally advanced solid tumors



ELIGIBILITY CRITERIA

- Relapsed/Refractory (R/R) or locally advanced, unresectable solid tumor for which no standard therapy exists
- Disease must be measurable per Response Evaluation Criteria
- Adult patients with an ECOG 0 or 1

PRIMARY MEASURES

- Determine safety and tolerability, maximum tolerated dose, recommended Phase 2 dose and dosing interval of RTX-240
- Assess pharmacodynamics (PD) of study treatment through changes in NK and T cell numbers relative to baseline

SECONDARY MEASURES

- Assess pharmacokinetics (PK) as measured the number of cells positive for both 4-1BBL and IL-15 using flow cytometry
- Determine anti-tumor activity as measured by overall response rate, duration of response, progression free survival and overall survival

*iv/it (intratumoral) dosing is designed with the combination of iv and it in cycle 1 followed by Q4W iv

Patient Characteristics – More Than 50% of Patients Had 3+ Prior Lines of Therapy

	TOTAL PATIENTS n=34
Median age, years (range)	58 (23-80)
Gender (Male/Female)	18/16
Ethnicity	
Non-Hispanic/Non-Latino	27
Hispanic/Latino	7
ECOG PS (0/1)	12/22
Most common primary site of cancer	
Non-small cell lung cancer (NSCLC)	8
Lower GI cancers[1]	8
Melanoma[2]	7
Renal cell carcinoma (RCC)	4
Other cancers[3]	7
Prior lines of systemic therapy in metastatic setting, median (range)[4]	3 (1-9)
1-2	15
≥3	18
Prior anti-PD-1/PD-L1 inhibitor therapy[4]	26
Anti-PD-1/PD-L1 + anti-CTLA-4 therapy[4-5]	11

[1]Lower GI cancers include anal cancer (n=3), colorectal cancer (n=2), gastroesophageal cancer (n=2), pancreatic ductal adenocarcinoma (n=1)
[2]Melanoma includes cutaneous melanoma (n=4), ocular melanoma (n=2), mucosal melanoma (n=1)
[3]Other cancers (all n=1), cervical, HNSCC, mesothelioma, ovarian, prostate, soft tissue sarcoma, testicular cancer
[4]One ongoing patient without reported prior cancer therapy at time of data-cut
[5]All patients who received prior anti-CTLA-4 therapy also received prior anti-PD-1/PD-L1 therapy either separately or in combination
Safety population: N=34 evaluable
Data cut-off: March 4, 2022

Continued Favorable Tolerability Results with No Treatment-Related Grade 3/4 AEs

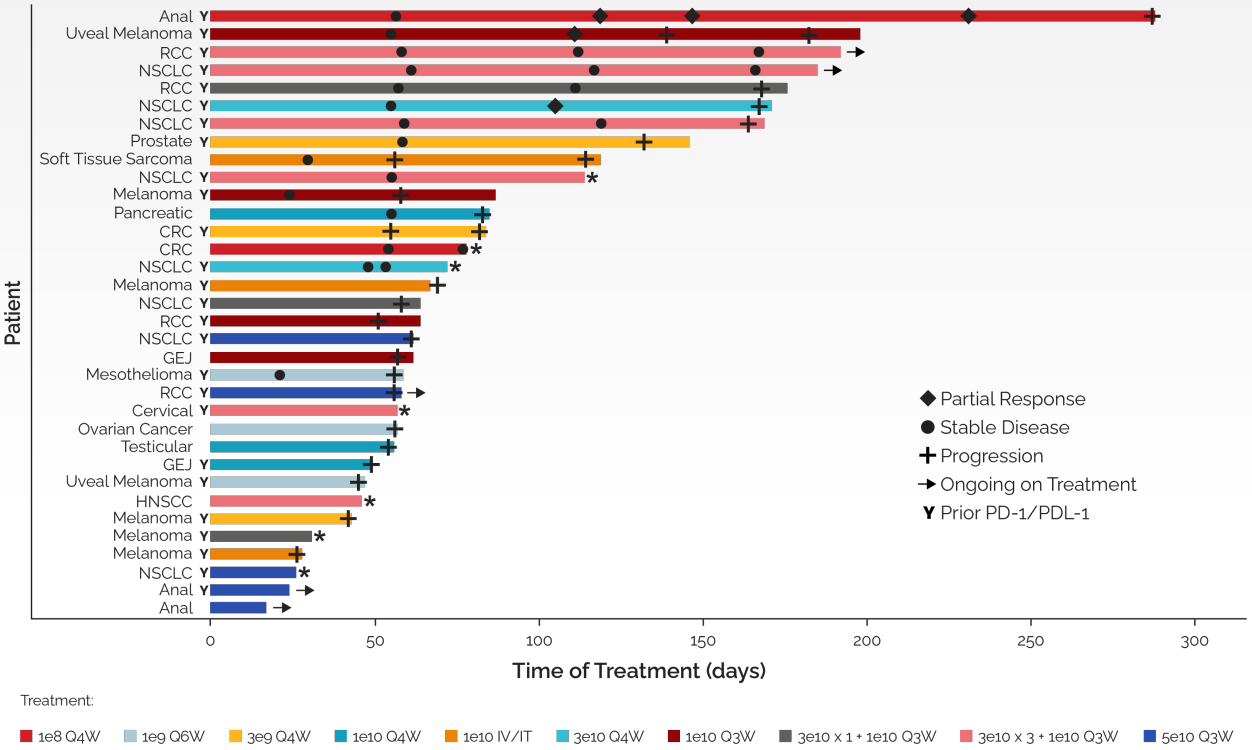
ADVERSE EVENT PREFERRED TERM	GRADE 1 n (%)	GRADE 2 n (%)	GRADE 3 n (%)	GRADE 4 n (%)	ANY GRADE n (%)
Fatigue	3 (9%)	2 (6%)	0	0	5 (15%)
Chills	3 (9%)	0	0	0	3 (9%)
Increased alanine aminotransferase	3 (9%)	0	0	0	3 (9%)
Nausea	3 (9%)	0	0	0	3 (9%)
Arthralgia	3 (9%)	0	0	0	3 (9%)
Decreased appetite	3 (9%)	0	0	0	3 (9%)
Pyrexia	2 (6%)	0	0	0	2 (6%)
Dysgeusia	2 (6%)	0	0	0	2 (6%)
Myalgia	2 (6%)	0	0	0	2 (6%)
Increased aspartate aminotransferase	2 (6%)	0	0	0	2 (6%)
Hyperhidrosis	2 (6%)	0	0	0	2 (6%)

Investigator Identified Immune-Related Adverse Events (irAEs)

- 21 Grade 1/2 irAEs were observed among 5 patients, no Grade 3/4 irAEs reported
- Grade 2 irAEs included adrenal insufficiency (n=1), fatigue (n=1), hypothyroidism (n=1), pneumonitis (n=1) and increased transaminases (n=1)

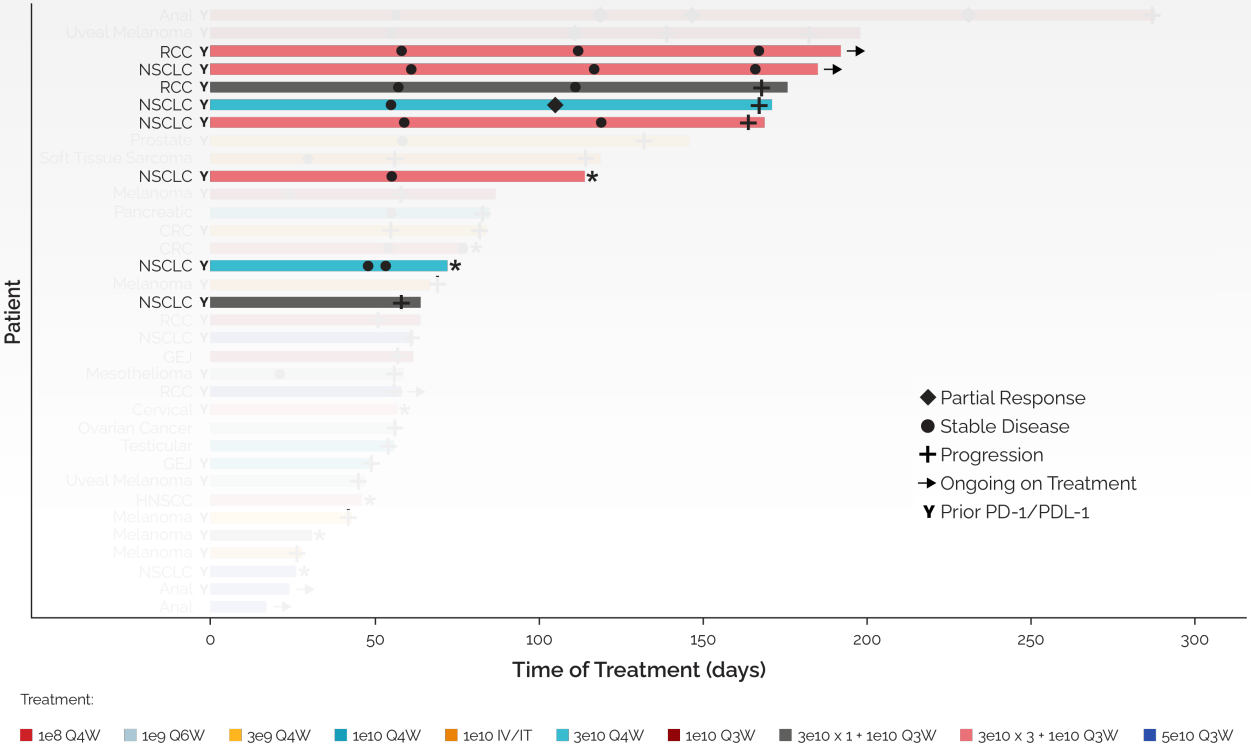
Data cut-off: March 4, 2022
Evaluable safety population: n=34
Treatment emergent adverse events by Grade related to RTX-240 (observed in 2 or more patients)
If an AE occurred more than once in same patient, the patient is counted once based on worst grade

Time on Treatment and Response in All Patients



RCC = renal cell carcinoma; NSCLC = non-small cell lung cancer; CRC = colorectal cancer; GEJ = gastroesophageal junction adenocarcinoma; HNSCC = head and neck squamous cell carcinoma
*Patient discontinued due to clinical disease (n=5) or death caused by disease progression (n=2) without radiological confirmation
Safety population: N=34 evaluable
Data cut: March 4, 2022

Unconfirmed Partial Response and 5 Cases of Stable Disease in Patients with NSCLC or RCC Across 3e10 Dose Cohorts



RCC = renal cell carcinoma; NSCLC = non-small cell lung cancer; CRC = colorectal cancer; GEJ = gastroesophageal junction adenocarcinoma; HNSCC = head and neck squamous cell carcinoma
*Patient discontinued due to clinical disease (n=5) or death caused by disease progression (n=2) without radiological confirmation
Safety population: N=34 evaluable
Data cut: March 4, 2022

Summary of Disease Control (SD ≥12 Weeks or PR)

TUMOR TYPE	PRIOR TREATMENTS	NUMBER OF PRIOR TREATMENTS	RTX-240 DOSE COHORT	BEST RESPONSE	TIME ON RTX-240 TREATMENT (DAYS)
Anal	Investigational anti-PD-L1 (LY3300005); investigational anti-ICOS antibody (KY1044) + atezolizumab	2	1e8 Q4W	PR	287^
Uveal Melanoma	Ipilimumab + nivolumab	1	1e10 Q4W	uPR	197
NSCLC	Carboplatin + nab-paclitaxel +atezolizumab	1	3e10 Q4W	uPR	170^
RCC	Paclitaxel + carboplatin; nivolumab	2	3e10 x 3 + 1e10 Q3W	SD	**191+**
NSCLC	Pembrolizumab	1	3e10 x 3 + 1e10 Q3W	SD	**184+**
RCC	Ipilimumab + nivolumab; nivolumab	2	3e10 + 1e10 Q3W	SD	175
NSCLC	Carboplatin + pemetrexed; investigational anti-PD-1 + investigational TIM-3 inhibitor; investigational antibody drug conjugate	3	3e10 x 3 + 1e10 Q3W	SD	168
Prostate	Abiraterone acetate + prednisone; enzalutamide + prednisone; docetaxel; docetaxel; tremelimumab + investigational anti PD-1 (PF-06801591) + investigational adenovirus gene therapy (AdC68)	5	3e9 Q4W	SD	145^
NSCLC	Cisplatin, pemetrexed; durvalumab	2	3e10 x 3 + 1e10 Q3W	SD	113
Pancreatic	L-leucovorin/5-FU + irinotecan + oxaliplatin	1	1e10 Q4W	SD	84

NSCLC = non-small cell lung cancer; PR = partial response; RCC = renal cell carcinoma; SD = stable disease; uPR = unconfirmed partial response
Date cut-off: March 4, 2022
^Time on RTX-240 longer than last line of therapy +Treatment ongoing

Summary of Disease Control (SD ≥12 Weeks or PR) in Patients with NSCLC or RCC

TUMOR TYPE	PRIOR TREATMENTS	NUMBER OF PRIOR TREATMENTS	RTX-240 DOSE COHORT	BEST RESPONSE	TIME ON RTX-240 TREATMENT (DAYS)
Anal	Investigational anti-PD-L1 (LY3300005); investigational anti-ICOS antibody (KY1044) + atezolizumab	2	1e8 Q4W	PR	287^
Uveal Melanoma	Ipilimumab + nivolumab	1	1e10 Q4W	uPR	197
NSCLC	Carboplatin + nab-paclitaxel +atezolizumab	1	3e10 Q4W	uPR	170^
RCC	Paclitaxel + carboplatin; nivolumab	2	3e10 x 3 + 1e10 Q3W	SD	**191+**
NSCLC	Pembrolizumab	1	3e10 x 3 + 1e10 Q3W	SD	**184+**
RCC	Ipilimumab + nivolumab; nivolumab	2	3e10 + 1e10 Q3W	SD	175
NSCLC	Carboplatin + pemetrexed; investigational anti-PD-1 + investigational TIM-3 inhibitor; investigational antibody drug conjugate	3	3e10 x 3 + 1e10 Q3W	SD	168
Prostate	Abiraterone acetate + prednisone; enzalutamide + prednisone; docetaxel; docetaxel; tremelimumab + investigational anti PD-1 (PF-06801591) + investigational adenovirus gene therapy (AdC68)	5	3e9 Q4W	SD	145^
NSCLC	Cisplatin, pemetrexed; durvalumab	2	3e10 x 3 + 1e10 Q3W	SD	113
Pancreatic	L-leucovorin/5-FU + irinotecan + oxaliplatin	1	1e10 Q4W	SD	84

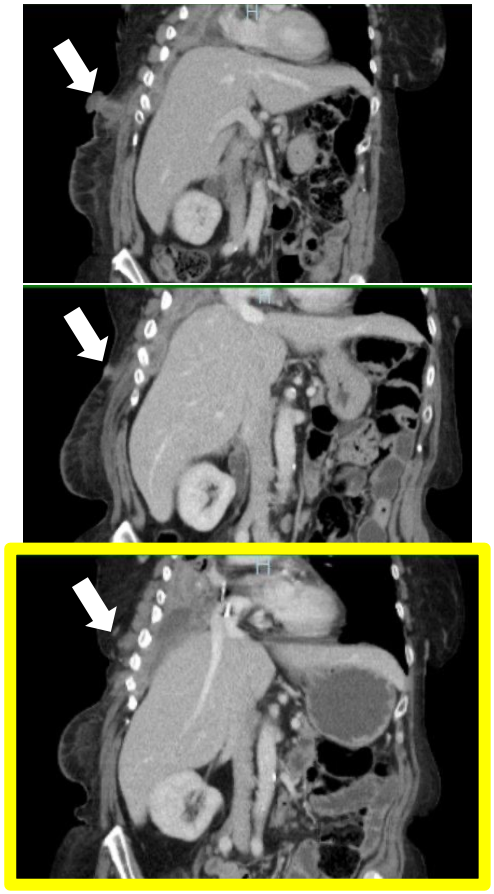
NSCLC = non-small cell lung cancer; PR = partial response; RCC = renal cell carcinoma; SD = stable disease; uPR = unconfirmed partial response
Date cut-off: March 4, 2022
^Time on RTX-240 longer than last line of therapy +Treatment ongoing

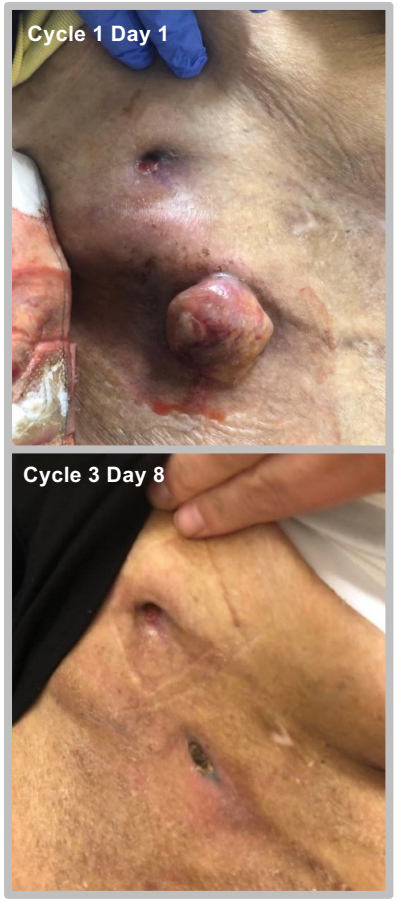
RubiusTherapeutics

PATIENT CASE STUDIES*

*Data cut-off March 4, 2022

Unconfirmed Partial Response in Non-Small Cell Lung Cancer





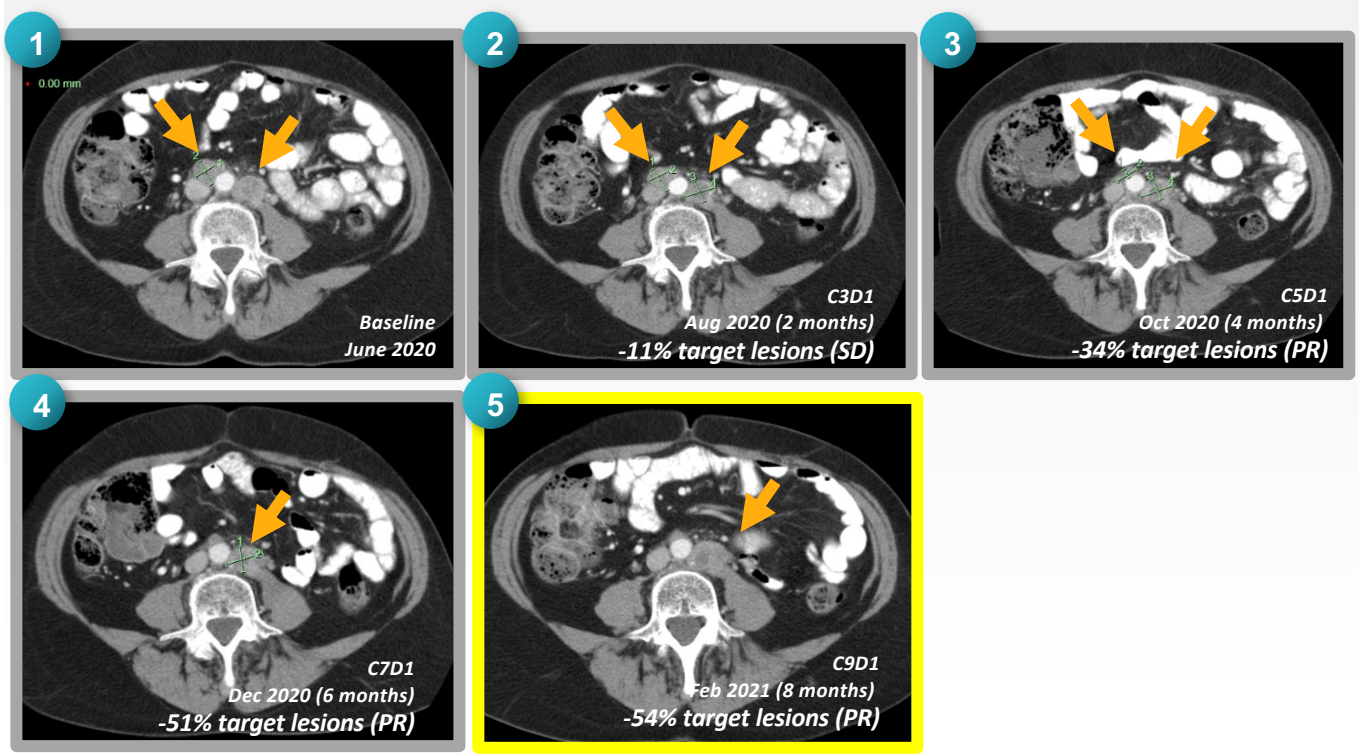
CASE HISTORY

- 69-year-old female (non-smoker) with metastatic non-squamous non-small cell lung cancer (PD-L1 score of 60%), including an external protruding right chest wall mass from site of prior chest tube
- **1L therapy** included surgery followed by **carboplatin + nab-paclitaxel + atezolizumab** and **atezolizumab** alone. Progressive disease (PD) prior to enrollment
- Received 6 cycles of RTX-240 3e10 cells IV every 4 weeks in **2L metastatic setting**
- Right chest wall mass dramatically decreased after 2 cycles of treatment
- An unconfirmed partial response was observed at Cycle 4 Day 22 with **-41% decrease of all target lesions** and duration of response (DOR) of 2 months
- Disease progression of non-target lesions after 5 months on-treatment

Confirmed Partial Response in Anal Cancer with 54% Reduction in Target Lesions

CASE HISTORY

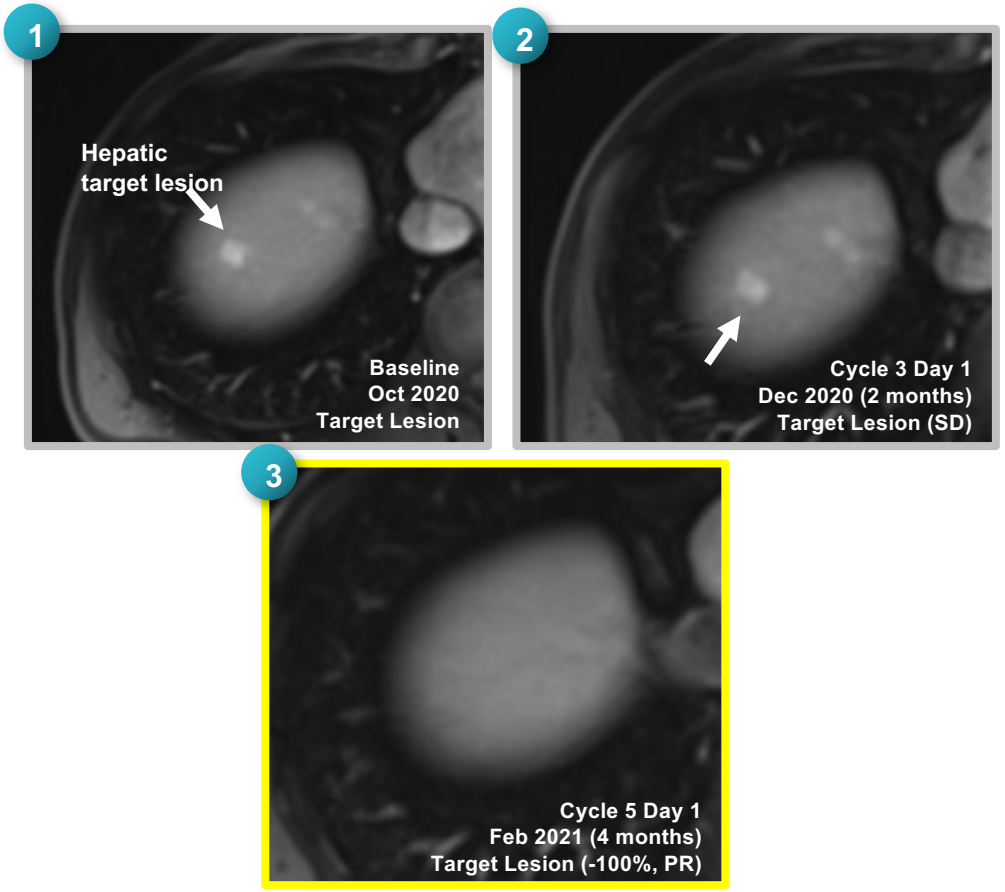
- 60-year-old female with squamous cell cancer of the anus
- Prior therapy included **1L anti-PD-L1** (LY3300054) for metastatic disease and **2L atezolizumab** (anti-PD-L1) with an experimental agonist (ICOS). PD prior to enrollment
- Treated with RTX-240 in the 1e8 Q4W IV cohort in **metastatic 3L setting**
- **54% decrease of target lesions** and DOR was 6 months
- PD after 10 months on-treatment



Unconfirmed Partial Response in Metastatic Uveal Melanoma with Complete Resolution of Hepatic Target Lesion at 16 Weeks

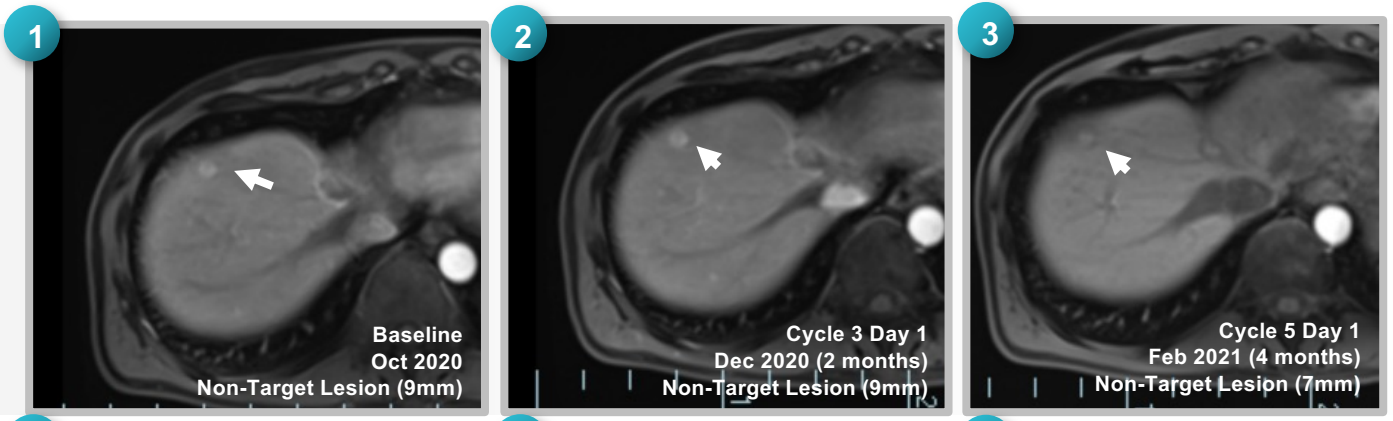
CASE HISTORY

- 54-year-old male with metastatic uveal melanoma; multiple hepatic metastases
- Treated with **nivolumab/ ipilimumab** in 1L metastatic setting. 8 months SD with PD prior to enrollment
- Treated with RTX-240 in 1e10 Q4W IV cohort in the **2L setting**
- **100% decrease in target lesion** and DOR was 1 month
- PD after 5 months on-treatment

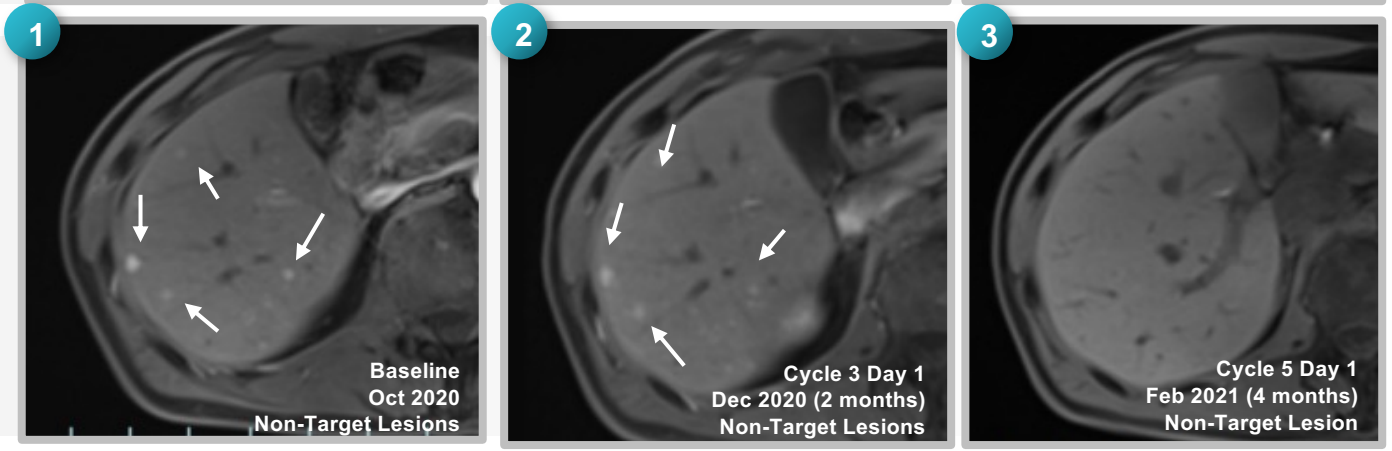


RTX-240 Induced Complete Regression of Multiple Lesions in the Liver in Metastatic Uveal Melanoma Patient

Upper liver images
Non-target lesions



Lower liver images
Non-target lesions



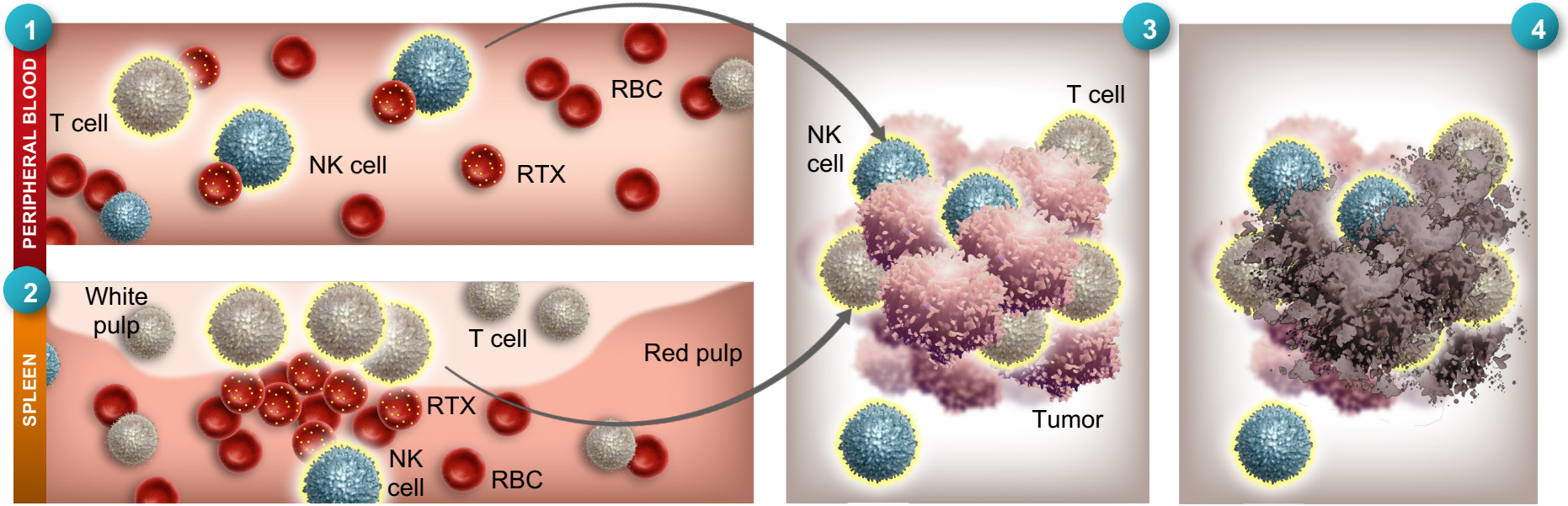
RubiusTherapeutics

PHARMACODYNAMIC DATA*

*Data cut-off January 29, 2022

RTX-240 Proposed Mechanism of Action

1 ACTIVATION | 2 EXPANSION | 3 TRAFFICKING | 4 TUMOR KILLING

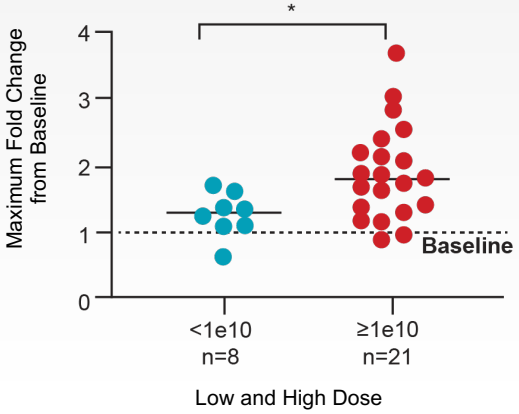


Potential for enhanced efficacy and safety versus agonists antibodies and recombinant cytokines by confining RTX-240 to the vasculature and spleen

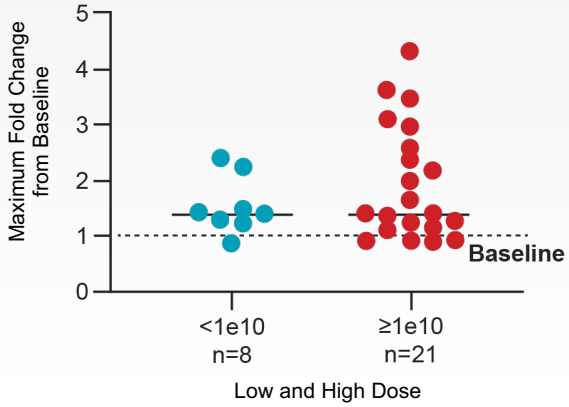
Dose Response Observed in Activation and Expansion of NK Cells

NK CELL ACTIVATION AND EXPANSION

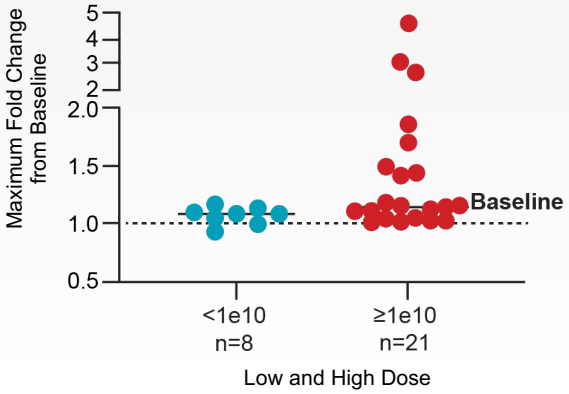
Maximum Fold Change in the Absolute Number of Circulating CD16/56+ NK Cells



Maximum Fold Change in the Percent of CD16/56+ NK Cells Expressing HLA-DR



Maximum Fold Change in the Percent of Memory CD16/56+ NK Cells Expressing Granzyme B



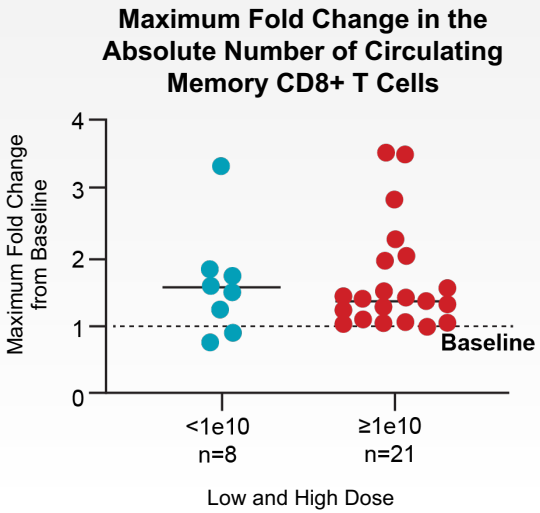
Low dose = 1e8-3e9 cells/dose (n=8); **High dose** = 1e10-3e10 cells/dose (n=21)

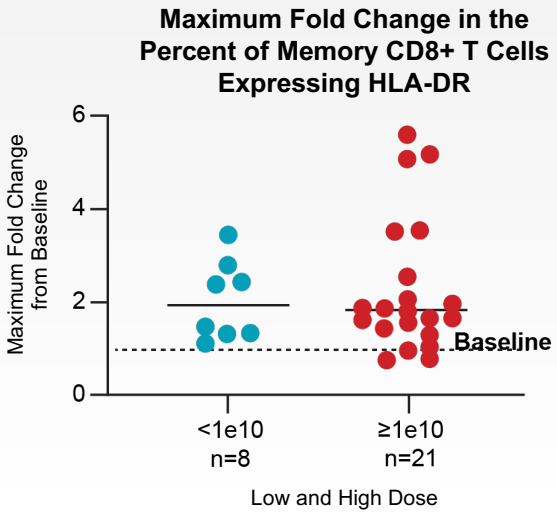
Statistically Significant Dose Response in NK Cell Expansion

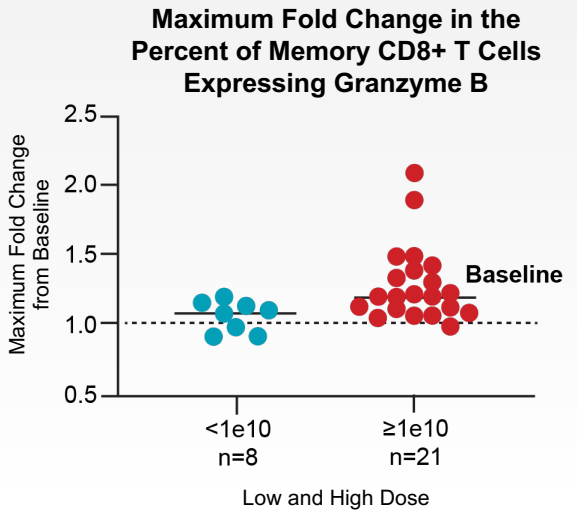
RubiusTherapeutics *p-value=0.049

Activation and Expansion of Memory CD8+ T cells

MEMORY CD8+ T CELL ACTIVATION AND EXPANSION





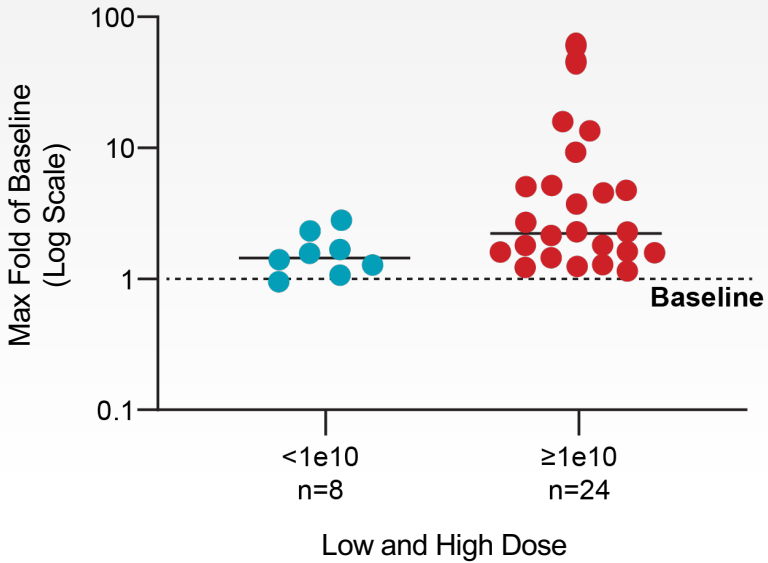


Low dose = 1e8-3e9 cells/dose (n=8); **High dose** = 1e10-3e10 cells/dose (n=21)

Activation or Increases in Memory CD8+ T Cell Numbers Observed in 90% of Patients

Increases in Circulating IFN-γ

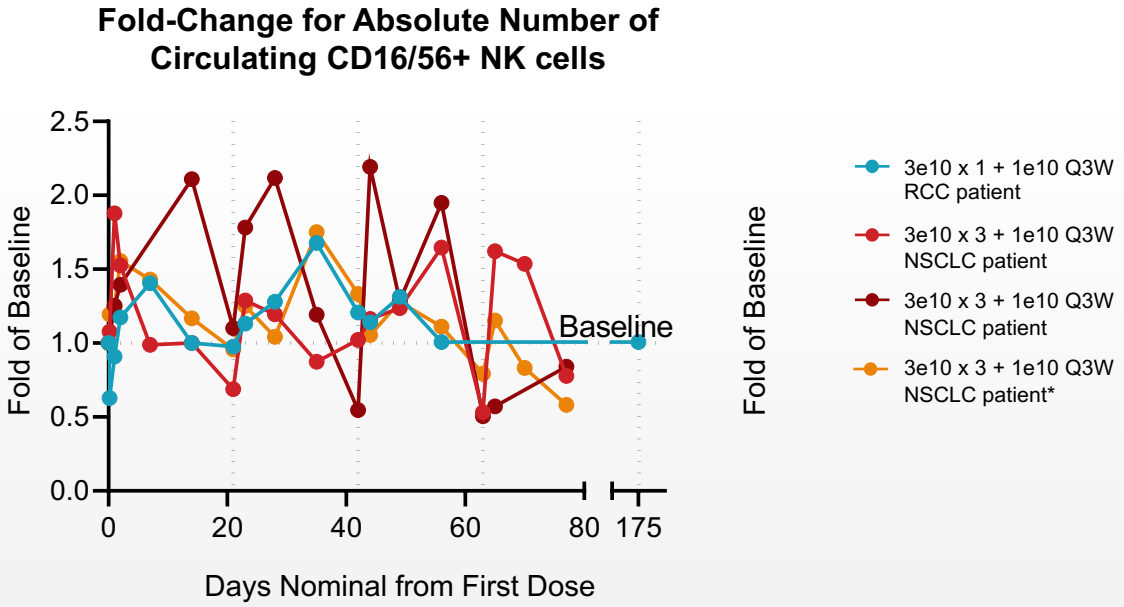
MAXIMUM FOLD CHANGE IN CIRCULATING LEVELS OF IFN-γ



Low dose = 1e8-3e9 cells/dose (n=8)
High dose = 1e10-3e10 cells/dose (n=24)

IFN-γ Produced by Activated T and NK Cells Drives Anti-Tumor Responses and Creates an Inflammatory TME

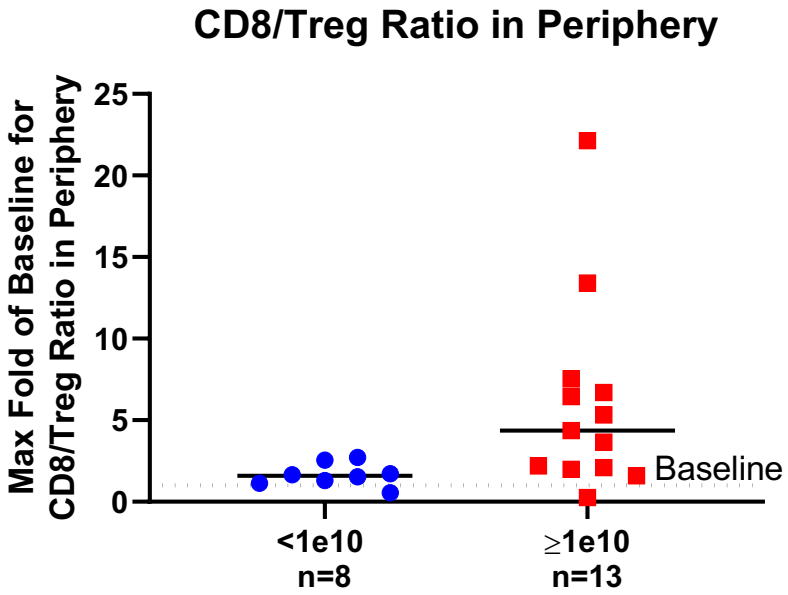
Kinetics of Pharmacodynamic Responses in NK Cells in Select Patients Dosed at 3e10



Kinetics of the target cell responses support Q3W dosing schedule

*Patient still on treatment at time of data cut-off of January 29, 2022

CD8/Treg Ratio in the Periphery



Nearly all patients (n=16/20)* had an increase in the CD8/Treg ratio (range, 1.5 - 22.0)

RTX-240 Stimulated Adaptive and Innate Immunity, Supporting Proof of Mechanism and Dosing

- Observed activation and/or expansion of NK or memory CD8+ T cells or both, the key target cell types of RTX-240, in all patients analyzed (n=29)
- Drove a statistically significant dose-response observed in NK cells numbers
- Increased percentages of memory CD8+ T cells and NK cells expressing the cytotoxic molecule Granzyme B
- Increased concentration of interferon-γ in plasma
- No effects observed on regulatory T cells (Tregs), which suppress effective tumor immunity
  - Nearly all patients (n=16/20)* had an increase in the CD8/Treg ratio (range, 1.5 - 22.0)
- Observed pharmacodynamic effects were long-lasting, supporting Q3 week dosing

*n=20 patients evaluated; Tregs were not measured in the first groups of patients enrolled in the trial

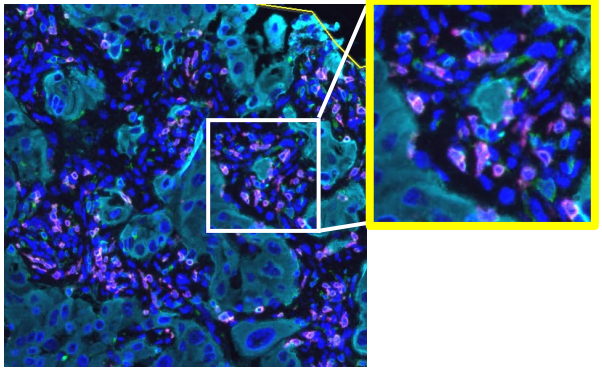
TUMOR TRAFFICKING DATA*

*Data cut-off January 29, 2022

Increase in Treatment-Related CD8+ T Cells in the Tumor Microenvironment of Patient with NSCLC at 3e10 Q4W

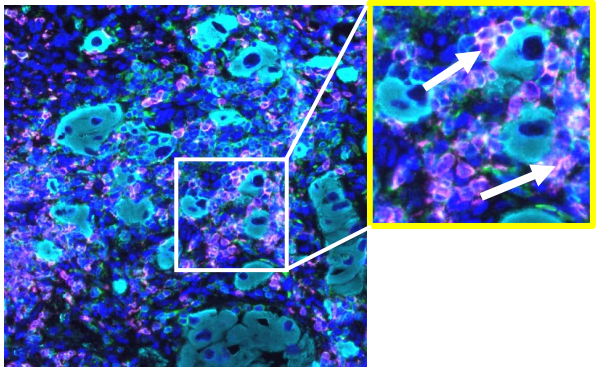
CK (Tumor)
CD8+ T Cell
CD3+ T Cells
Nucleus

A.



Baseline biopsy

B.



On-treatment biopsy (C2D8)

Immune Populations of Interest in Tumor Microenvironment	Baseline, %	On-Treatment, % (Fold Increase)
% CD8+ T Cells of all cells (CD3+/CD8+)	8.9	33.1 (3.7-fold)
CD8+ Cell Density (cells/mm^2)	316	1420 (4.5-fold)

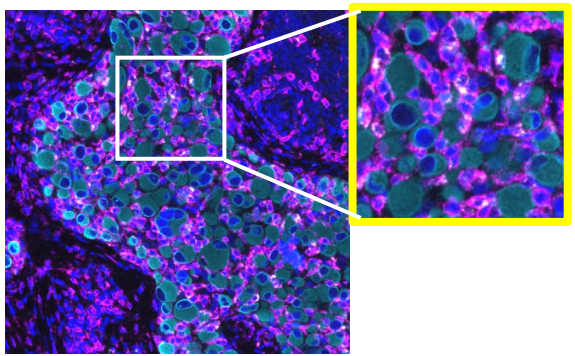
- RTX-240 promoted trafficking of CD8+ T cells into the tumor microenvironment in a patient with metastatic NSCLC
- (A) Baseline biopsy obtained at screening and (B) on-treatment biopsy with **>4-fold increase in density** of CD8+ T cells observed

Arrows = CD3+CD8+ T cells in close proximity to the tumor. Starting with strong CD3 and CD8 overlap appears white. Images collected and analyzed by Ultivue using 12-plex I/O TIL panel.

Increase in Treatment-Related CD8+ and Granzyme B+ CD8+ T Cells in Tumor Microenvironment of Patient with RCC at 3e10 + 1e10 Q3W

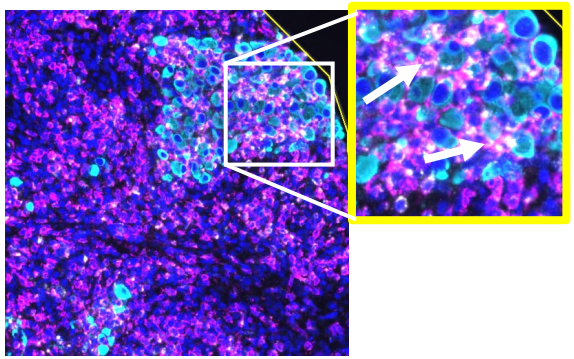
CK (Tumor marker)
CD8 (T Cell)
Granzyme B
Nucleus

A.



Baseline biopsy

B.



On-treatment biopsy 1 (C2D9)

Immune Populations of Interest in Tumor Microenvironment	Screening	On-Treatment, % (Fold Increase)
% Granzyme B+ CD8+ T Cells of all cells (CD3+CD8+GrB+)	5.5	9.9 (1.8-fold)
Granzyme B+ CD8+ T Cell Density (CD8+GrB+ cells/mm^2)	316	828 (2.2-fold)
CD8+ T Cell Density (CD3+CD8+ cells/mm^2)	1786	3704 (2.1-fold)

- Increases in CD8+ and Granzyme B+ CD8+ T cells observed in tumor microenvironment in lymph node biopsy in a patient with metastatic RCC treated with RTX-240
- (A) Baseline biopsy at baseline and (B) on-treatment biopsy with **~2-fold increase in density** of CD8+ T cells and Granzyme B+ CD8+ T cells in regions of tumor

Arrows = Granzyme B+ and CD8+ T cells. Images collected and analyzed by Ultivue using 12-plex I/O TIL panel.

Tumor Trafficking from Periphery into the Tumor Microenvironment

- Trafficking of both T and/or NK cells was observed in 4/6 patients from collected biopsies* (1.6 to 10-fold increases)
  - Shown in patients (1 each) with NSCLC, renal cell carcinoma, metastatic mesothelioma and metastatic soft tissue sarcoma
- Increase in CD8+ T cells positive for the tumor-killing molecule Granzyme B expression in 3/6 patients with solid tumors
  - Highlights improved cytotoxic potential of T cells within TME
- Increased expression of PD-L1 and/or increased ratio of M1/M2 macrophages observed in 3/6 patients with solid tumors
  - Suggests improved immune-permissive TME, which may enhance innate and adaptive tumor-associated immune cell responses

*Biopsies were not mandated per the study protocol

RubiusTherapeutics

RTX-240 CLINICAL DEVELOPMENT PLAN

Rationale for RTX-240 in Combination with Checkpoint Inhibitors for NSCLC and RCC

- Updated clinical data indicate that RTX-240 warrants further development as combination therapy with checkpoint inhibition
  - Expanding Phase 1 arm of RTX-240 + pembrolizumab to focus on NSCLC and RCC patients
  - Informing future Phase 2 combination trial of RTX-240 + pembrolizumab
- Favorable tolerability results of RTX-240
- Trafficking of T cells to the TME is highly predictive of responses to PD-1 inhibition*
  - Early evidence of improved immune-permissive TME with increased expression of PD-L1 after treatment with single-agent RTX-240
- RTX-240 activated both T and NK cells and PD-1 is a common checkpoint in both T and NK cells in human tumors
- Potential for synergistic effects between RTX-240 and pembrolizumab that could activate and expand target cells in the periphery
  - Once cells are activated by RTX-240 and enter the TME, pembrolizumab may sustain their activity by delaying or preventing T cell exhaustion

*Wu, TD, et al. Grogan JL. Peripheral T Cell Expansion Predicts Tumour Infiltration and Clinical Response. *Nature* 2020

Focusing Phase 1 Arm of RTX-240 + Pembrolizumab to NSCLC and RCC to Inform Phase 2 Trial

RTX-240 & Pembrolizumab

RELAPSED/ REFRACTORY(R/R) SOLID TUMORS

TUMOR TYPE

Enrollment continues

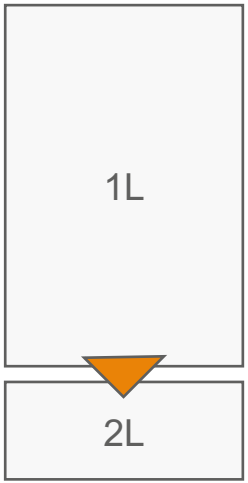
Planned

	PHASE 1: First-in-Human Dose Escalation	**PHASE 1: INFORMING PHASE 2**	**PHASE 2**
DEVELOPMENT PLAN	1e9 + PD-1 Q3W n=4 → 3e9 + PD-1 Q3W n=3 → 1e10 + PD-1 Q3W n=3 → 5e10 + PD-1 Q3W n=3	5e10 + PD-1 Q3W (n=up to 20)	RP2D + PD-1 Q3W
TUMOR TYPE	• Relapsed/refractory or locally advanced solid tumors • "All comers"	• Non-small cell lung cancer • Non-clear cell renal carcinoma	
ELIGIBILITY CRITERIA	• 1-3 prior lines of therapy • Patients must have disease that is relapsed or refractory to an anti-PD-1 or PD-L1 therapy	• Patients who have experienced disease progression with 1-2 prior treatment regimens in the metastatic setting or refuse or are unable to tolerate standard treatment • If prior PD-(L)1 regimen, a prior response to checkpoint inhibitor is required (SD≥6 months, PR or CR)	

No Dose-Limiting Toxicities Observed to Date

Following Disease Progression in NSCLC on IO Therapy, Limited Clinical Benefit from Alternative Treatment Options

Decline in ORR and PFS from 1L to 2L treatment in NSCLC



	ORR (%)	mPFS (months)
Pembrolizumab (TPS* >50%)[1]	**39-45**	**6.5-7.7**
Pembrolizumab (TPS* >1%)[2]	**27**	**5.5**
Pembrolizumab + chemo (non-squamous NSCLC)[3]	**50-62**	**9**
Pembrolizumab + chemo (squamous NSCLC)[4]	**63**	**8**
Docetaxel [5,6,7]	**9-20**	**3-4**

2L+ unmet need

- Only agent for 2L NSCLC is **docetaxel** with **limited benefit** and **significant toxicity**
- **Less than 50%** of Stage 4 NSCLC patients **receive 2L treatment**

1 KEYNOTE-024 and KEYNOTE-042; 2 KEYNOTE-042; 3 KEYNOTE-189; 4 KEYNOTE-407; 5 Hanna et al., J Clin Oncol. 2004 May 1;22(9):1589-97; 6 Ramlau et al., J Clin Oncol. 2012 Oct 10;30(29):3640-7
7 Alexis Vergnenegre et al., J Thorac Oncol. 2011 Jan;6(1):161-8

RTX-240 Opportunity in Evolving NSCLC Treatment Landscape

CURRENT NSCLC TREATMENT PARADIGM

- **Pembrolizumab-based regimens are SOC for 1L**
  - Pembro + chemo in patients with TPS <50%
  - Pembro monotherapy often used for high PD-L1 expressors
  - Significant opportunity for improved outcomes
- In **2L therapy**, patients have limited options
  - Additional chemotherapy – docetaxel – with limited PFS/OS benefit

OPPORTUNITY

- Development in combination with pembrolizumab leverages favorable tolerability profile of RTX-240 to potentially generate clinical benefit
- 1L therapy with RTX-240 + pembro ± chemotherapy
- 2L therapy with RTX-240 +/- docetaxel

RTX-240 Opportunity in Evolving Non-Clear Cell RCC Treatment Landscape

CURRENT RCC TREATMENT PARADIGM

- Agents used to treat RCC are approved irrespective of disease histology
- Registrational studies **excluded patients with nccRCC**
- No consensus SOC beyond 1L for nccRCC (typically TKI therapy[1])
- Therapies indicated for RCC are expected to **provide less therapeutic benefit in nccRCC** than in ccRCC
- **ICIs present potential to enhance clinical benefit in 1L nccRCC**

OPPORTUNITY

- Development in combination with pembrolizumab leverages favorable tolerability profile of RTX-240 to potentially enhance 1L SOC treatment or expand to other settings and combinations
- 1L RTX-240 + pembrolizumab + TKI
- Treatment of patients who have responded but progressed after initial ICI ± TKI treatment

1 Cabozantinib is considered 1L SOC and has demonstrated ORR of 23%, mPFS of ~9 months, mOS of ~20 months, with 74% of patients experiencing Grade 3/4 Aes (study enrolled papillary nccRCC patients only)

Clinical Development Journey and Efficacy Benchmarks for Select IO Therapies

		ORR	Stable Disease Rate
LAG-3 inhibitors	Monotherapy	0%[1]	0-48%[2]
	ICI combination	3-67%[3]	9-45%[4]
TIGIT inhibitors	Monotherapy	0-3%[5]	17-32%[6]
	ICI combination	3-69%[7]	18-50%[8]

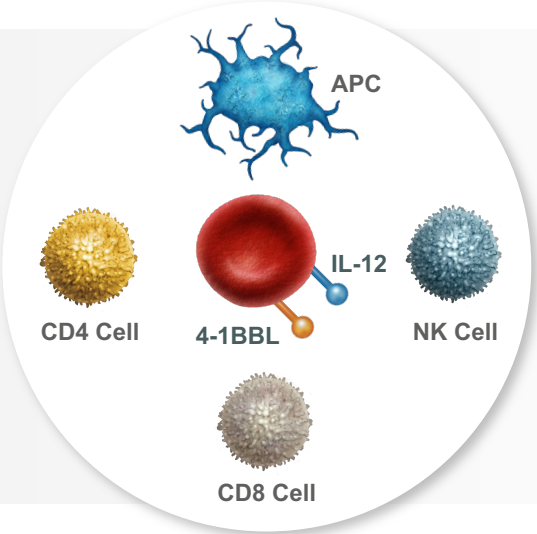
1 In heavily pre-treated patients; data reported for favezelimab (Merck) in Microsatellite Stable Colorectal Cancer (MSS CRC) and fianlimab (REGN) in R/R solid tumors; monotherapy ORR undisclosed for relatlimab (BMS) and efti alpha (Immutep)
2 Favezelimab (0% SD) in R/R MSS CRC; fianlimab (48% SD) in R/R solid tumors
3 Favezelimab (3% ORR) combination pembrolizumab, in previously treated, advanced microsatellite stable CRC patients with TPS < 1%; fianlimab (67% ORR) combination with cemiplimab, in PD-(L)1 naïve melanoma (all TPS)
4 Fianlimab (9% SD) combination with cemiplimab, in PD-(L)1 naïve melanoma (TPS unselected), but note that ORR was 67%; relatlimab (45% SD) combination with nivolumab, in PD-(L)1 refractory melanoma (all TPS)
5 Tiragolumab (Roche, 0% ORR) in R/R solid tumors/ heavily pre-treated patients; vibostolimab (Merck, 3% ORR) in PD-(L)1 refractory NSCLC (all TPS)
6 Tiragolumab (17% SD) and vibostolimab (32% SD) in R/R solid tumors/ heavily pre-treated patients
7 Vibostolimab (3% ORR) combination with pembrolizumab, in PD-(L)1 refractory NSCLC (all TPS); tiragolumab (69% ORR) in combination with atezolizumab, in 1L NSCLC (TPS ≥ 50%)
8 Vibostolimab combination with pembrolizumab, in 1L NSCLC, SD rate of 18% (TPS < 1%) and 50% (TPS ≥ 1%)

RubiusTherapeutics

RTX-224: BROAD IMMUNE STIMULATION

RTX-224: Broad Immune Stimulation with Two Agonist Pathways. Dosed First Patient in Q1'22

BROAD IMMUNE STIMULATION



ENHANCED TUMOR KILLING
BY ACTIVATING CD8+ AND CD4+ T CELLS AND NK CELLS

BROAD IMMUNE SYSTEM
STIMULATION LEADS TO ENHANCED ANTIGEN PRESENTATION

POTENTIAL BENEFITS:

- Replicate immune system function to activate four key target cell types: CD4+ and CD8+ T cells, APCs and NK cells
- Induce immune activation and antigen presentation for a broad and effective anti-tumor response

Differentiation of RTX-240 and RTX-224 Based on Proposed Mechanism of Action

RTX-240

- Mechanism of action of **RTX-240** involves two key concepts:
  - Activation and expansion of **NK cells** in the peripheral blood and spleen
  - Activation and expansion of **memory CD8+ T cells** in the peripheral blood and spleen

RTX-224

- Mechanism of action of **RTX-224** involves three key concepts:
  - Strong **T cell activation** of both **CD4+ Th1 cells** and **CD8+ T cells**
  - Activation of **antigen presentation** through differentiation of antigen-presenting cell
  - Retains the ability to activate NK cells
- Suitable for tumors that are responsive to checkpoint inhibition and/or have high mutational burden

RTX-240 and RTX-224 MOAs lead to

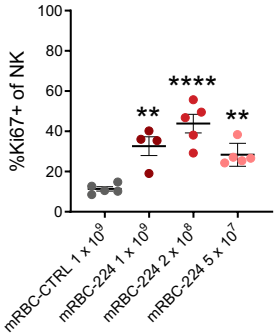
- Trafficking of T and NK cells to the tumor microenvironment (TME)
- Flip in the immune status of the TME from immuno-suppressive to immuno-permissive

mRBC-224 Induces Activation of Target-Cell Populations in Blood and Spleen in Lung Metastases Melanoma Model

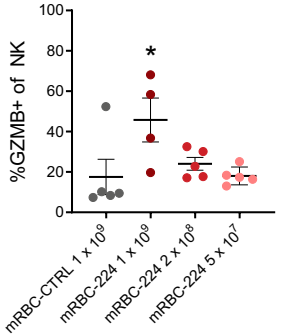
Blood staining on day 14 after 4 doses on days 1,4,8,11. similar results are seen in spleen

NK CELLS

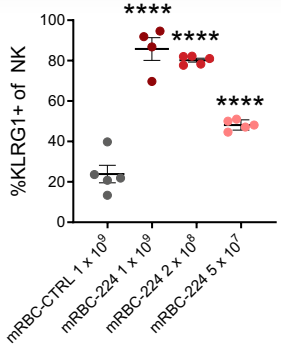
Proliferation



Cytotoxicity

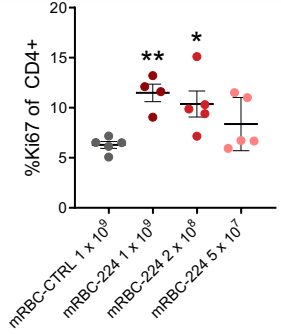


Differentiation



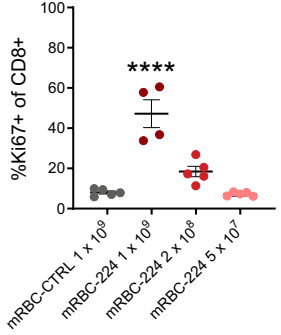
CD4+ T CELLS

Proliferation

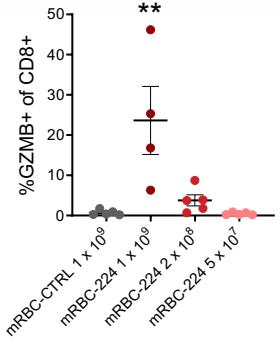


CD8+ T CELLS

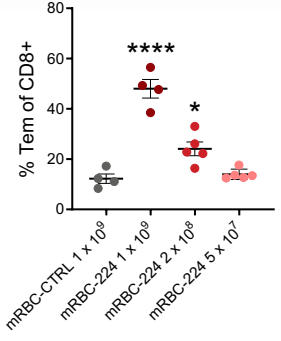
Proliferation



Cytotoxicity

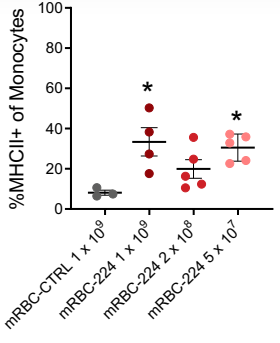


Differentiation



MONOCYTES

Activation

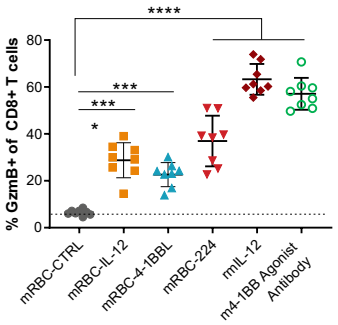


mRBC-224 Induces Activation of Target Cells in the Tumor Microenvironment in Lung Metastases Melanoma Model

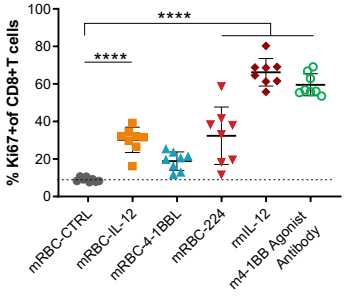
- Mice harboring lung metastases of B16F10 tumors were treated with 3 doses Q3D of mRBC-224 (murine surrogate of RTX-224)
- Changes in target immune cell populations observed in the lung (site of metastasis)

CD8+ T CELLS

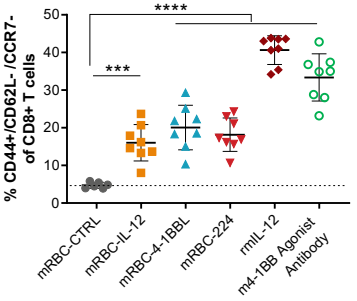
Cytotoxicity



Proliferation

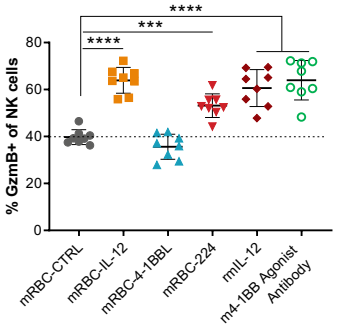


Differentiation

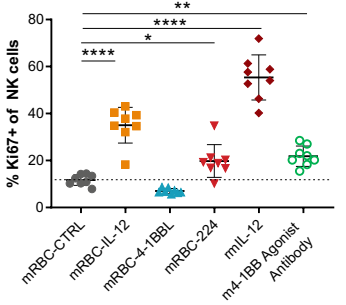


NK CELLS

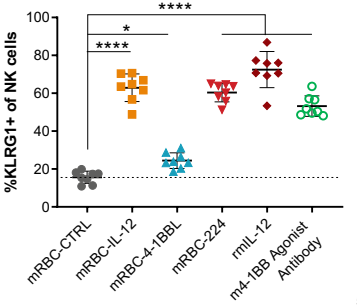
Cytotoxicity



Proliferation



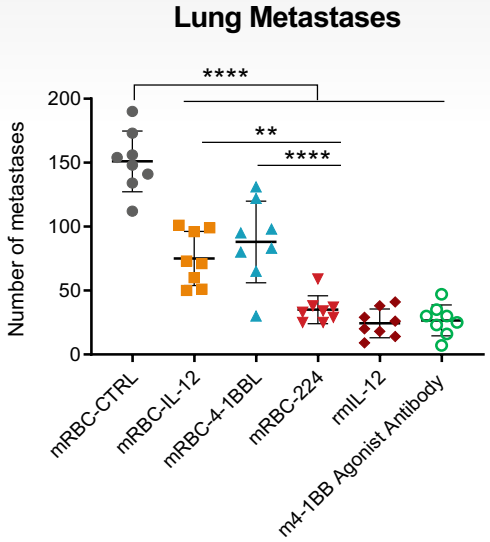
Differentiation

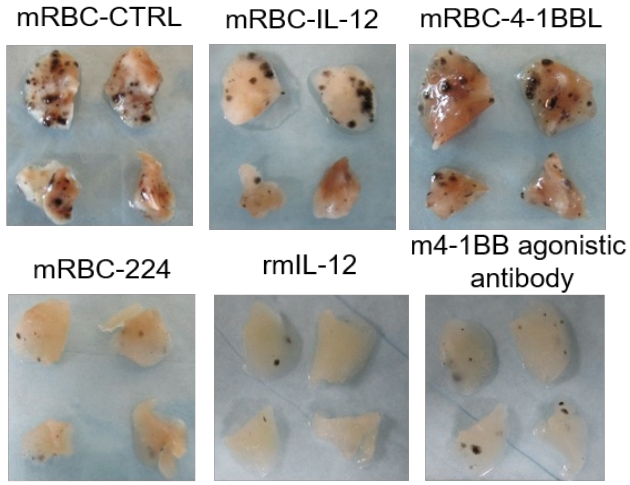


mRBC-224 Significantly Reduces B16 Lung Metastases

RTX-224 EFFICACY | (4-1BBL + IL-12)

- Mice harboring lung metastases of B16F10 tumors were treated with 3 doses Q3D of mRBC-224 (murine surrogate of RTX-224)
- Lung metastases were significantly inhibited by mRBC-224 and the effects of IL-12 and 4-1BBL were additive

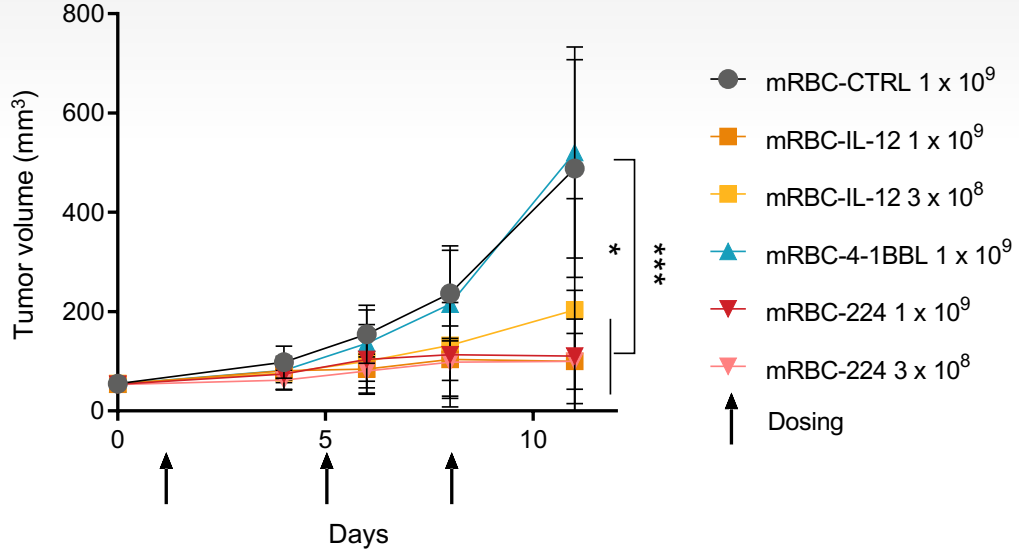




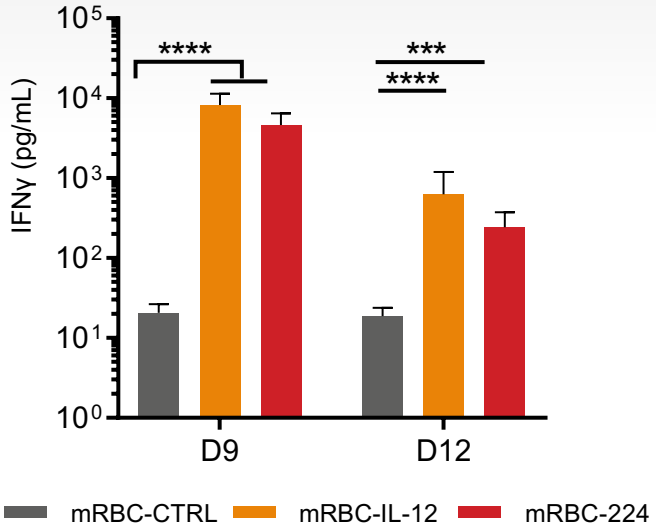
Dugast, A et al. (2019) RTX-224, an Allogeneic Red Cell Therapeutic Expressing 4-1BBL and IL-12, Exhibits Potent In Vitro and In Vivo Activity and a Favorable Preclinical Safety Profile *American Association for Cancer Research*

mRBC-224 Significantly Inhibits Tumor Growth in MC38 Colorectal Cancer Model and is Associated with Increase in Serum IFNγ

mRBC-224

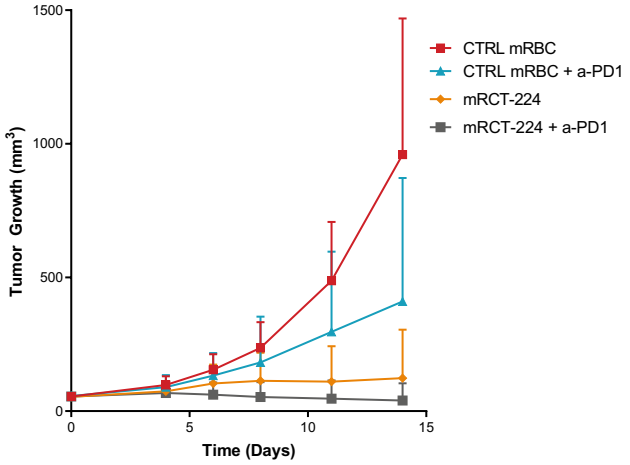


SERUM IFNγ

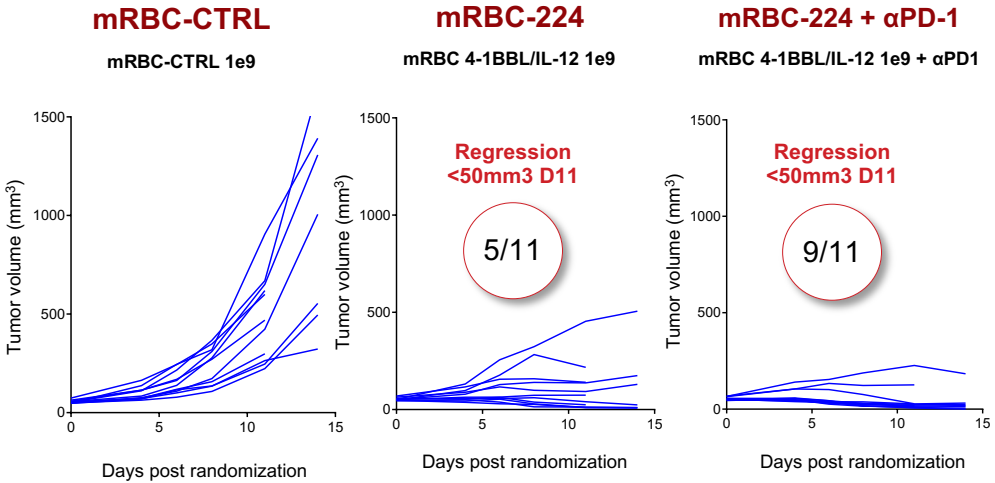


mRBC-224 Efficacy in MC38 Colorectal Cancer Model Tumor Model

EFFICACY MC38 MODEL



ROBUST TUMOR REGRESSIONS



Strong efficacy as single agent and in combination

Dugast, A et al. (2019) RTX-224, an Allogeneic Red Cell Therapeutic Expressing 4-1BBL and IL-12, Exhibits Potent In Vitro and In Vivo Activity and a Favorable Preclinical Safety Profile *American Association for Cancer Research*

RTX-224 Clinical Development Plan in Select Advanced Solid Tumors

METASTATIC CANCERS*
CUTANEOUS MELANOMA
HNSCC
UROTHELIAL CANCERS
NSCLC
TNBC

Enrolling: Phase 1 Dose Escalation

Phase 2 Expansion Specific Indication(s)

1e8 Q3W	5e8 Q3W	1e9 Q3W	5e9 Q3W	1e10 Q3W	Further explore dose and interval

KEY INCLUSION CRITERIA

- Disease progression following standard combination platinum- or mitomycin C-based chemo and PD-1/PD-L1 therapy
- No prior immune-related adverse events (irAE) of Grade 3 or higher and resolution of all irAEs to Grade ≤1

PRIMARY MEASURES

- Determine the safety and tolerability of monotherapy RTX-224 and RP2D

SECONDARY MEASURES

- Assess PD changes in immune cell populations in peripheral blood and tumor biopsies
- Determine anti-tumor activity of RTX-224 as measured by ORR, duration of response, progression free survival and overall survival

RubiusTherapeutics

*HNSCC: Head & Neck Squamous Cell Carcinomas; NSCLC:, Non-Small Cell Lung Cancer; TNBC: Triple Negative Breast Cancer

RubiusTherapeutics

TOLERANCE INDUCTION FOR AUTOIMMUNE DISEASE

Autoimmune Rationale & Strategy

Validate RED PLATFORM beyond oncology and potentially disrupt standard of care in autoimmune diseases

Large Unmet Need in Autoimmunity

Significant opportunity to change standard of care and address needs in many autoimmune diseases

- Competitive approaches have limited efficacy and significant side effects
- Superior safety profile vs. broad-spectrum immunosuppressants
- Expected durability of protective effect (low frequency dosing, higher quality of life)

Approach

Exploit the ability of red cells to induce tolerance

- Utilize Rubius' programmable platform to express autoimmune antigens in or on RCTs for T cell-mediated diseases

Mechanism of action translatable to multiple autoimmune diseases, including type 1 diabetes, multiple sclerosis and celiac disease

Prioritizing Type 1 Diabetes, Multiple Sclerosis and Celiac Disease: High Potential T Cell-Mediated Diseases

	Type 1 Diabetes (T1D)	Multiple Sclerosis	Celiac Disease
US Target Segment	**~60K (annually) with new onset**	**~360K (prevalence) mild, moderate, relapsing remitting**	**~150K (prevalence) non-responsive to diet**
Scientific Rationale	Multiple confirmed antigenic drivers	Multiple confirmed antigenic drivers	Single antigen disease driver
Unmet Need	No approved disease-modifying therapies	High need for safe treatment	Greatest unmet need primarily in gluten-free diet refractory / non-responsive disease, and broader demand may exist
Development Favorability	Established development pathway with clear clinical benchmarks	Established development pathway with clear clinical benchmarks	Early surrogate marker available

Source: Physician Interviews; Payer Interviews; ClearView analysis

RTX-T1D, A Potential Disease-Modifying Therapy: Scientific Rationale and Clinical Considerations

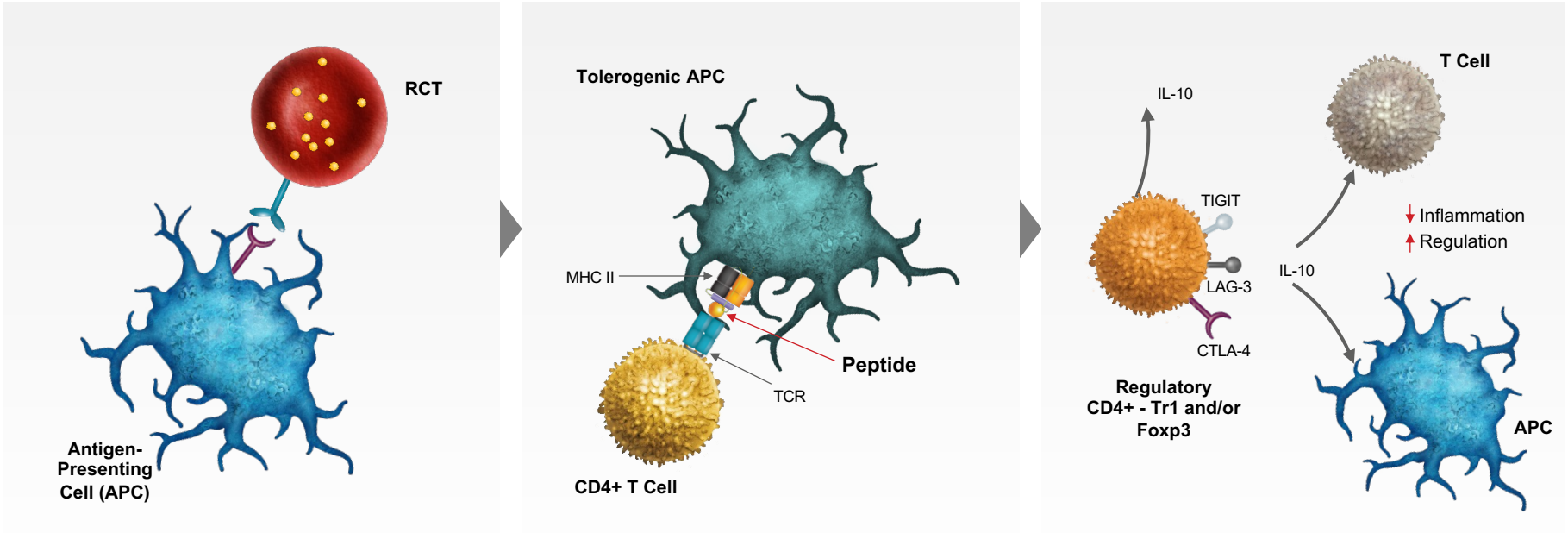
Scientific Rationale	• T1D is a T cell-driven autoimmune disease with defined antigens making it a good target for Rubius' antigen-specific tolerance therapy
Experimental Highlights	• Achieved durable efficacy in two models of T1D • Efficacy associated with striking upregulation of two key types of regulatory T cells and down regulation of effector T cells, providing proof of mechanism
Clinical Considerations	• No approved disease modifying therapies • Need for safe therapies that reverse the autoimmune process, prevent beta cell destruction and preserve insulin production • Clinical approaches: Treatment of early disease and prevention in high-risk patients

Mechanism of Action for Targeting APCs to Induce Tolerance is Well Established

1 RCTs naturally processed by APCs

2 Tolerogenic APCs engage CD4 cells

3 CD4+ regulatory T cells drive tolerance

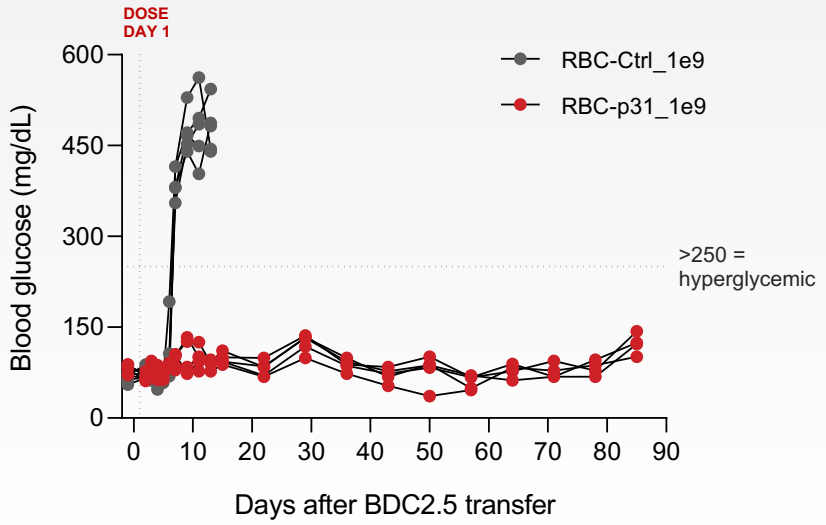


This mechanism applies to all Rubius autoimmune target indications

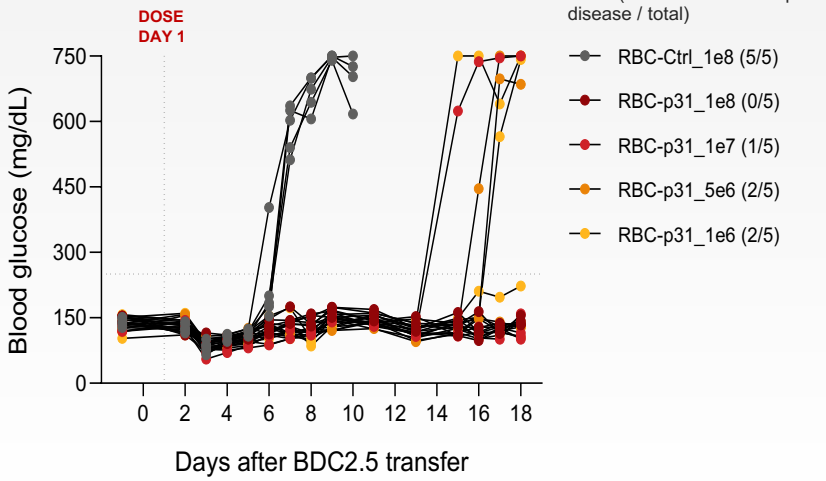
Pearson et al., *Adv Drug Deliv Rev.* 2017, 114:240-255
Serra & Santamaria, Nat Biotechnol. 2019, 37(3):238-251
Shepard et al., Front. Immunol., 2021, 12:1168

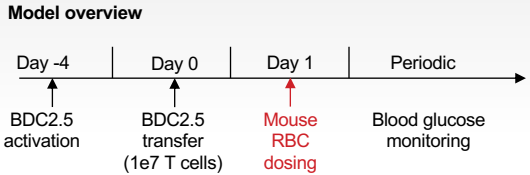
Antigen-Conjugated Mouse RBCs Prevent Diabetes with a Single Dose

LONG-TERM CONTROL (1e9)



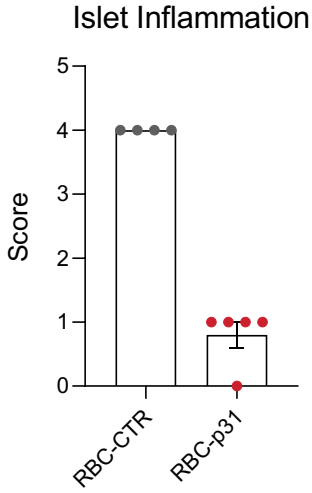
LOW DOSE EFFICACY (1e8 to 1e6)

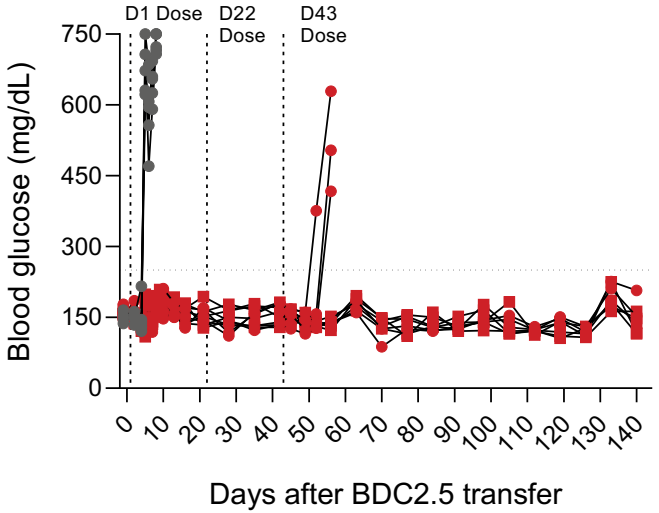




Low-Dose Retreatment Prevents Disease Onset in Diabetes Model

- Mice dosed with 1e8 p31-RBC displayed insulitis on Day 18 after BDC2.5 cell adoptive transfer
- With a Day 22 and Day 43 repeat dosing we can extend the protection compared to a single dose at Day 1
  - Mice in multi-dose group have increased Treg/Teffector ratio



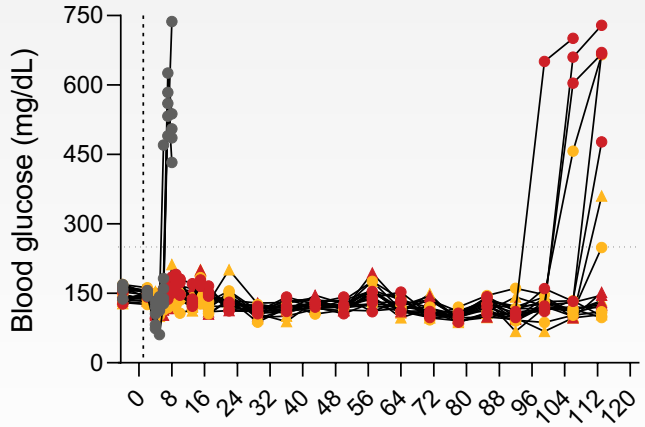


RBC-Ctrl (5/5)
RBC-p31^{Single} (3/5)
RBC-p31^{Multi} (0/5)

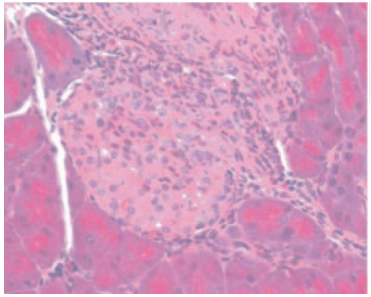
Diabetes prevented in all 5 animals for 5 months

Treatment is Effective even when Tissue Inflammation is Established - a Relevant Model for Human Autoimmunity

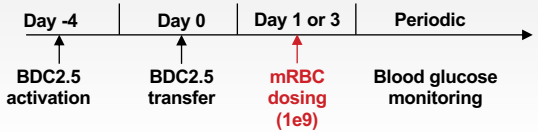
DOSING DAY 1 VS. DAY 3 IN BDC2.5 DIABETES MODEL



RBC-Ctrl
RBC-p31, 1e9
RBC-p31, 2e8
D1
RBC-p31, 1e9
RBC-p31, 2e8
D3



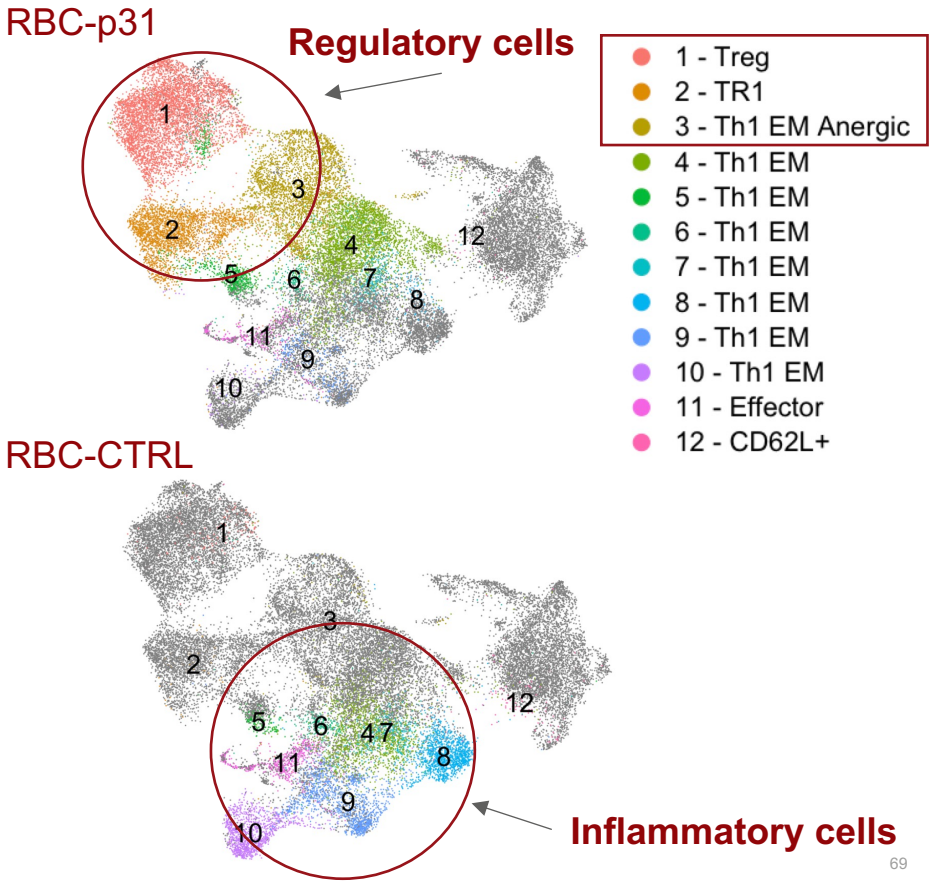
Inflammation evident on Day 3



Rubius Mouse RBCs Induce Regulatory T Cells – RNAseq Analysis

CD4+ T cells from RBC-p31-treated mice create Treg, Tr1 and anergic cells, which are absent in RBC-CTRL treated mice

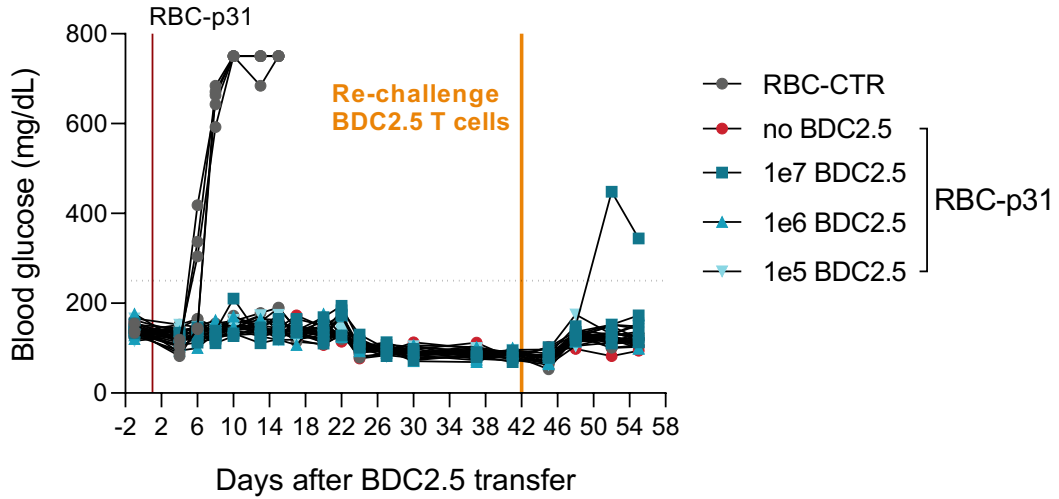
- Rubius mRBCs lead to the development of regulatory T cells
- Regulatory T cells prevent effector cells from mounting an immune response and will be required for successful antigen-specific treatment of autoimmune disease



Treg and TR1 – Regulatory T cells
TH1 EM – T helper type 1 cells, effector memory

Previously Tolerized Mice are Protected from Re-Challenge

Day 42 Re-Challenge of Tolerized Mice



Treated mice are immune from re-challenge with diabetes-causing T cells

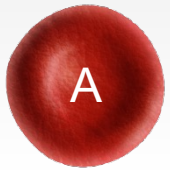
Non-Obese Diabetes (NOD) Model of Type 1 Diabetes

A strain of mice called NOD mice develop spontaneous diabetes

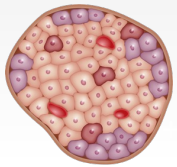
The genetics and biology of this disease are remarkably similar to human T1D

- Disease develops spontaneously
- Is associated with peri-insulitis (T cells surrounding islets) and then frank insulitis with beta cell destruction
- Multiple auto-antigens are involved
- NOD mice have a unique MHC class II gene with a similar sequence to a high susceptibility human MHC Class II gene
- Both patients with type 1 diabetes and NOD mice have polymorphisms in multiple genes affecting regulatory T cells

WHAT IS BYSTANDER SUPPRESSION?
A process by which tolerance induced to one antigen is extended to other antigens expressed on the same tissues



RCT engineered to express antigen “A”

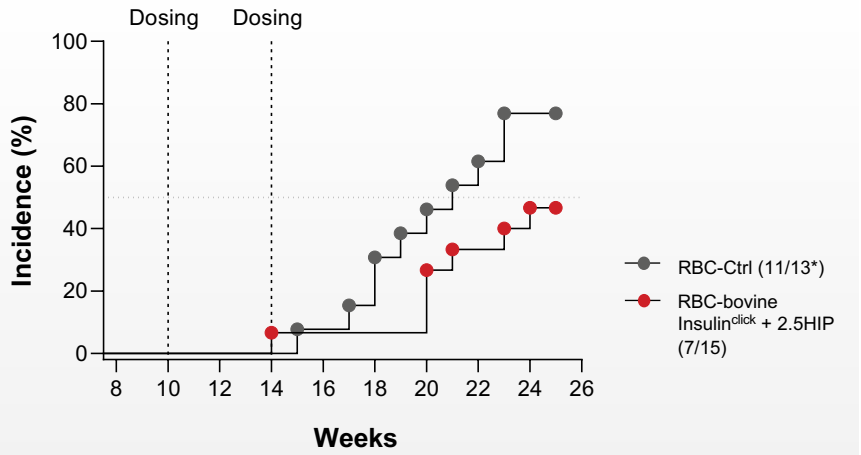


Antigens A + B

A patient no longer has an autoimmune response to either antigen A **or antigen B.**

Antigen B is the “bystander” and tolerance to antigen A has spread to other antigens

Mouse RBCs Delay and Prevent Disease in NOD Model



*Two mice expired early in the experiment before development of diabetes

Diabetes incidence at 25 weeks of age

Genetics and biology of NOD model remarkably similar to human T1D

- Disease develops spontaneously
- Associated with peri-insulitis (T cells surrounding islets) and then frank insulitis with beta cell destruction
- Multiple auto-antigens are involved
- Unique MHC class II gene with similar sequence to human MHC Class II gene
- Both T1D patients and NOD mice have polymorphisms affecting regulatory T cells

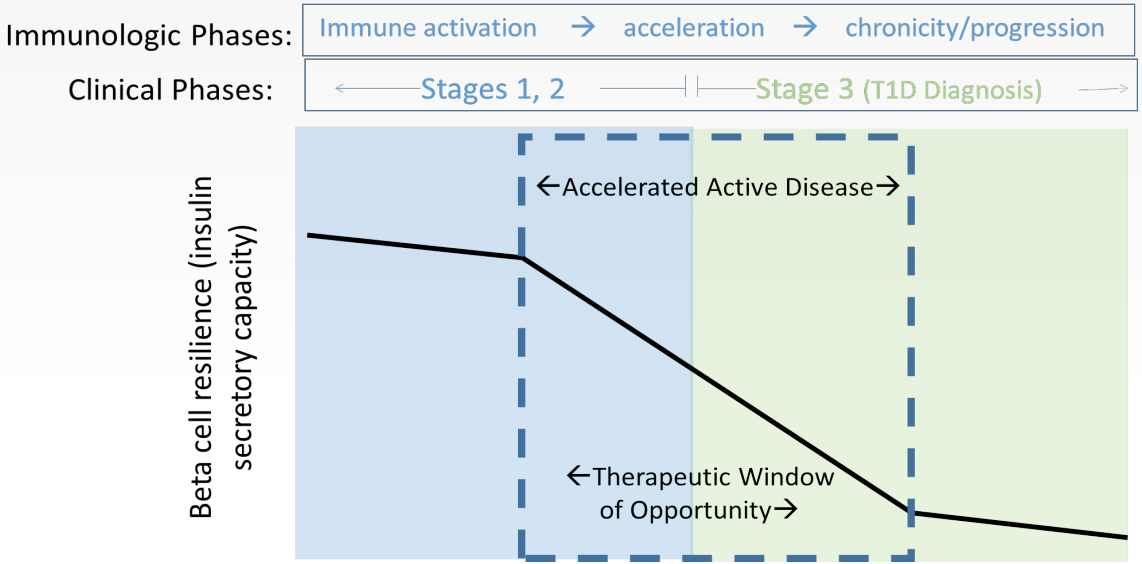
- Results at 25 weeks demonstrate bystander suppression by delivering only two antigens
- mRBC-T1D prevented or delayed disease caused by many auto-antigens

Clinical Development for Type 1 Diabetes (T1D)

T1D Clinical Trials Highly Standardized for Efficient Drug Development:

- A metabolic outcome biomarker (secreted c-peptide) of residual beta cell function;
- A readily identifiable recently-diagnosed patient population;

Prospects for early intervention/prevention prior to clinical diagnosis



Autoimmune Summary

Programmable platform enables unique ability to direct and the modulate immune system to generate tolerance

Preclinical proof of concept in Type 1 diabetes models validates approach and applies to multiple autoimmune diseases

Established efficacy in the BDC2.5 adoptive transfer model:

- Repeated dosing extended the duration of disease protection
- Reversed established inflammation, important for patients with existing autoimmunity
- Induces two types of regulatory T cells, resulting in protection against re-challenge

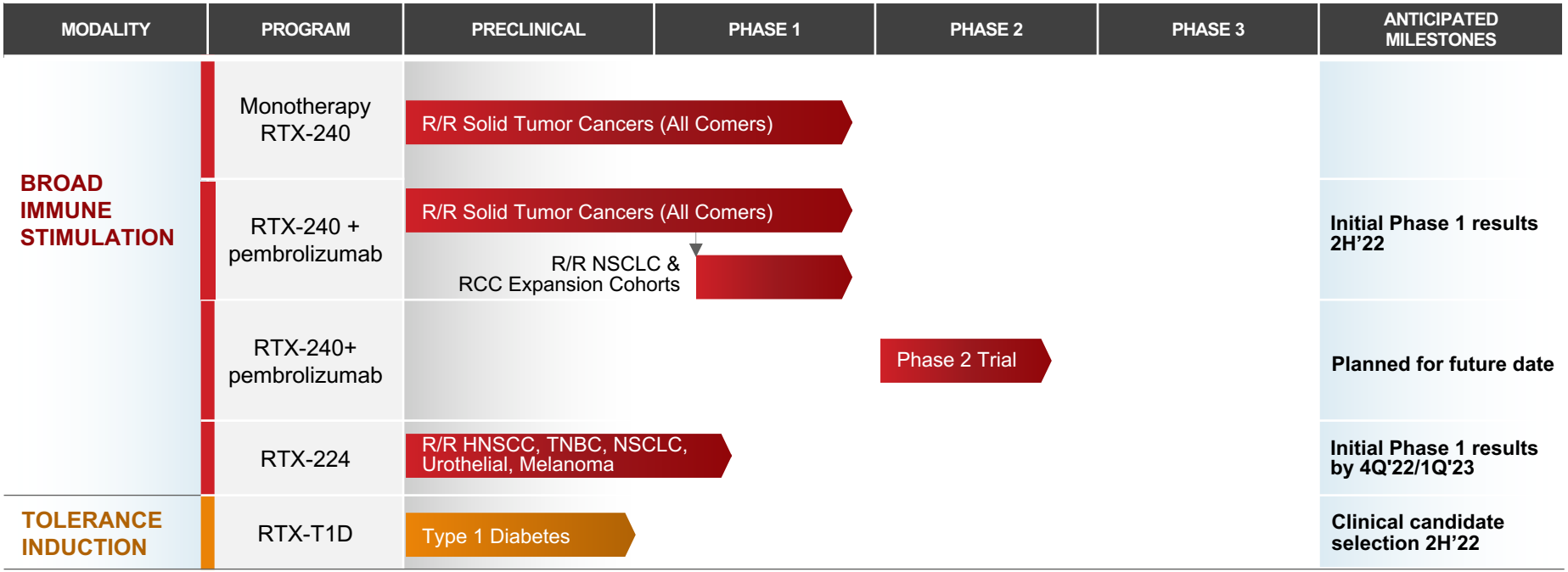
Established effectiveness in Non-Obese Diabetic mice

Advancing RTX-T1D towards an IND application

Rubius Therapeutics

PIPELINE & EXPECTED CATALYSTS

Anticipated Milestones from Rubius' Broad Wholly Owned Pipeline



Expanding ongoing Phase 1 arm of RTX-240 + pembrolizumab to focus on NSCLC and RCC patients to inform Phase 2 clinical trial

NSCLC = Non-small cell lung cancer; NHSCC = Head and neck squamous cell carcinoma; RCC = Renal cell carcinoma; TNBC = Triple negative breast cancer

RubiusTherapeutics

REALIZING THE POWER OF RED™
A NEW ERA IN CELLULAR MEDICINE

Rubius Therapeutics

APPENDIX

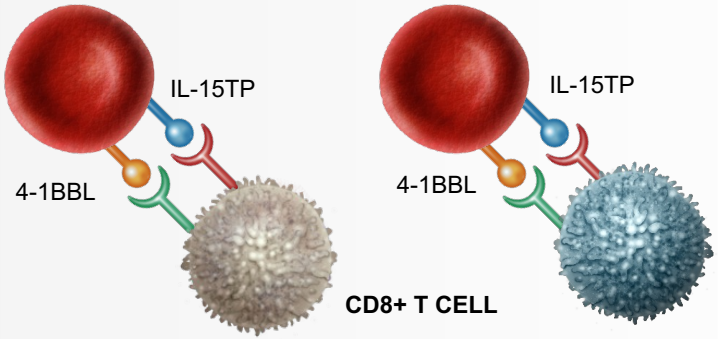
RubiusTherapeutics

RTX-240: PRECLINICAL DATA

RTX-240 is Designed to Deliver Two Key Agonist Signals to the Immune System – Currently Enrolling Three Phase 1 Arms

BROAD IMMUNE SYSTEM STIMULATION

RTX-240 | (4-1BBL + IL-15TP)



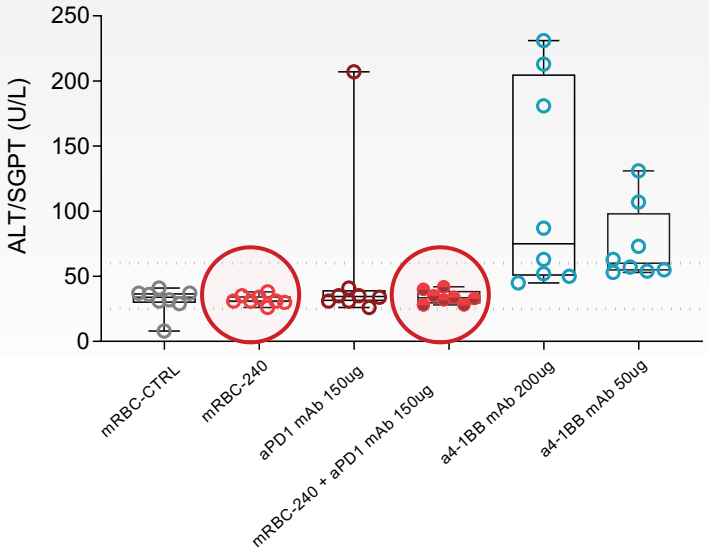
DESIGNED TO **STIMULATE** ADAPTIVE AND INNATE IMMUNE CELL AGONIST PATHWAYS

POTENTIAL BENEFITS:

- Activate existing agonist pathways leading to enhanced potency
- Overcome resistance to immunotherapy
- Reduce toxicity given biodistribution confined to vasculature and spleen, widening the therapeutic window of agonists

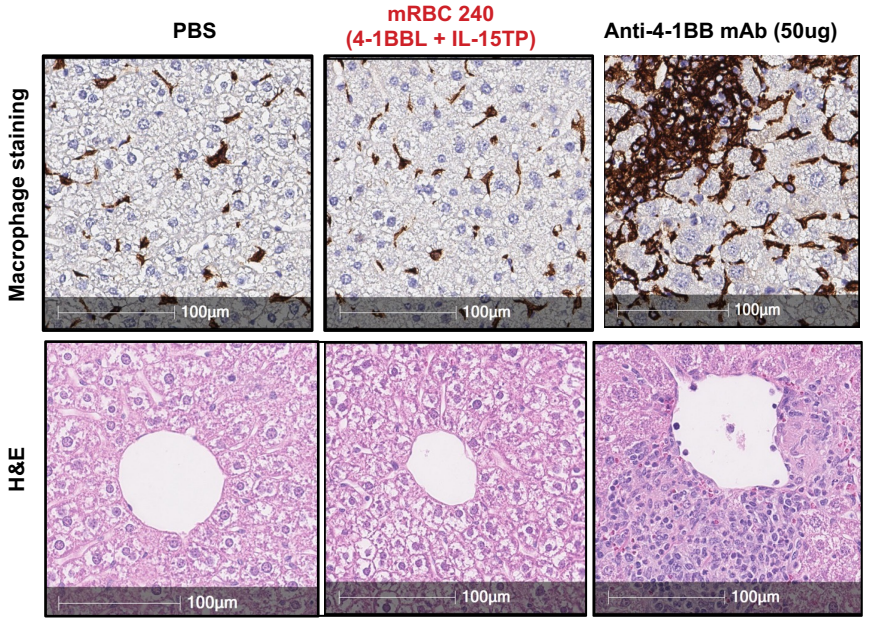
mRBC-240 Results in No Liver Toxicity Compared to Anti-4-1BB mAb

SERUM ALT



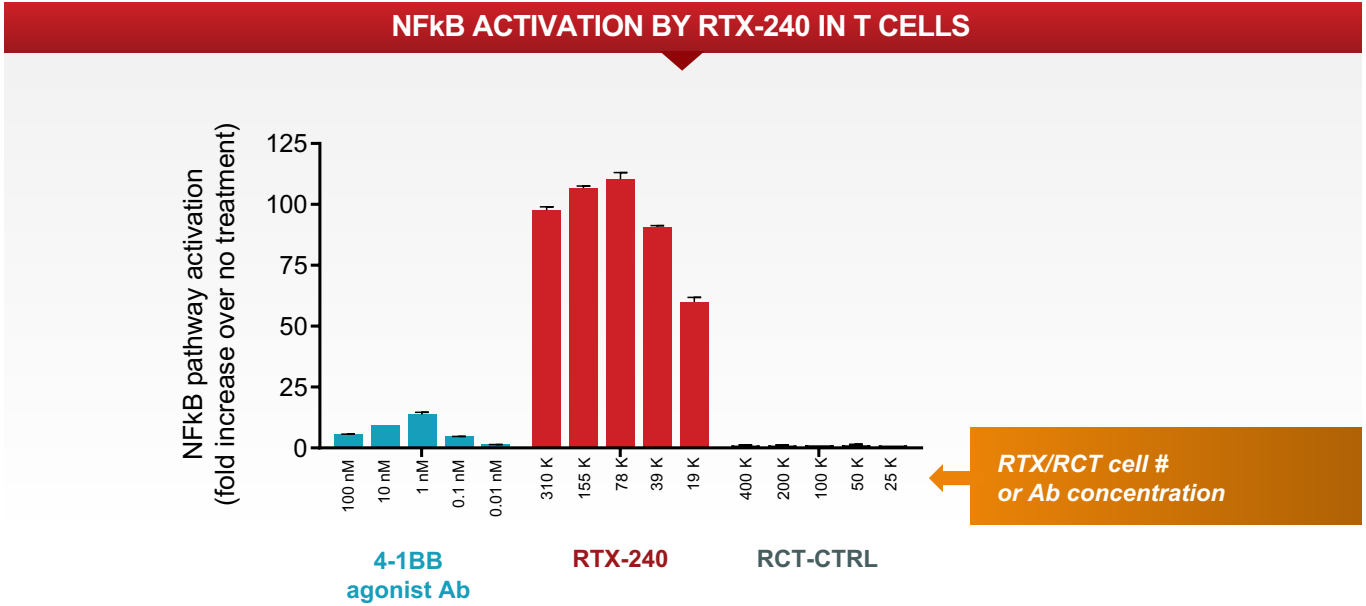
Normal mice; 4 Doses, 1x10^9 cells day 0, 3, 7, 10; Sacrifice day 18

LIVER HISTOLOGY



Dugast, et. al., *American Association for Cancer Research*; Poster #3272, 2019

RTX-240 Stimulated Potent Activation of Immune System In Vitro

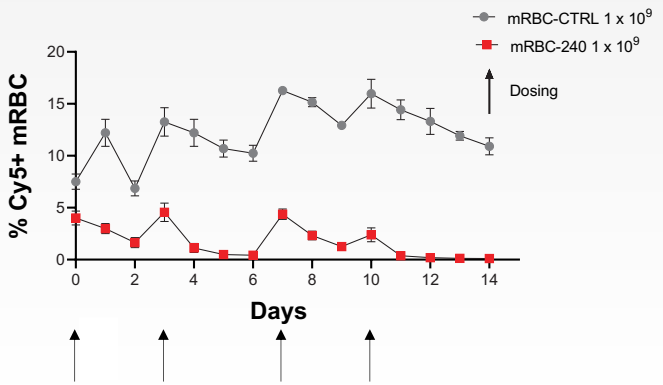


RTX-240 is ~10-Fold Superior to 4-1BB Agonist Antibody in Preclinical Models

Dugast, et. al., *American Association for Cancer Research*; Poster #3272, 2019

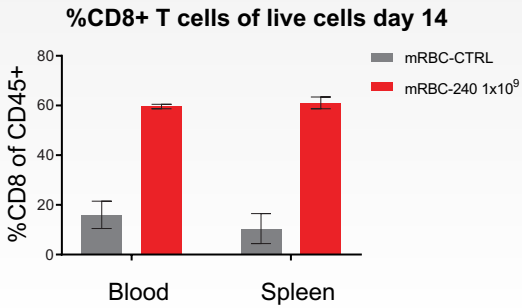
Treatment with mRBC-240 Expands CD8 and NK Cell Numbers in Spleen and Blood

PK OF mRBC-CTRL AND mRBC-240

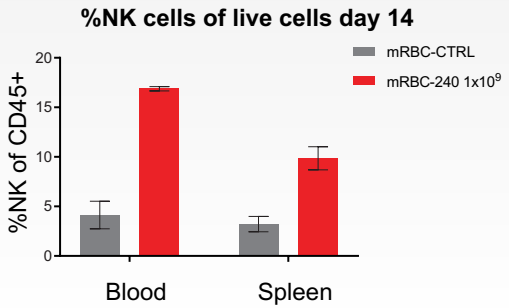


EFFECTS IN THE SPLEEN AND BLOOD ON DAY 14

CD8 T Cells



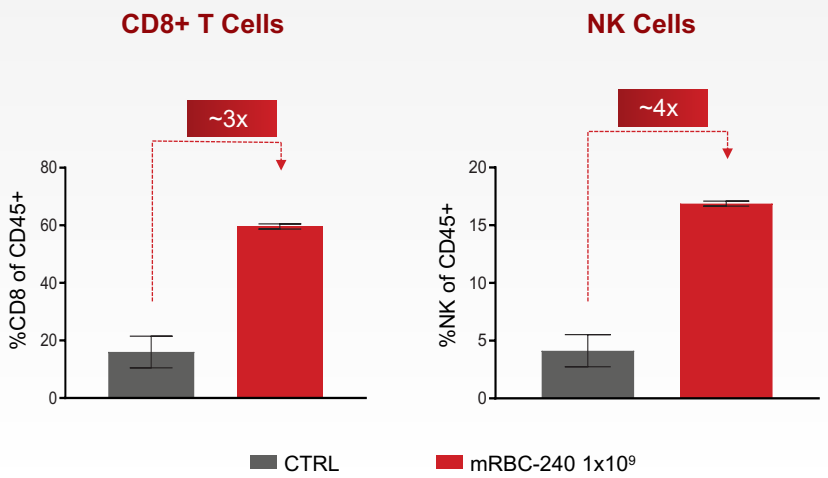
NK Cells



Normal mice; 4 Doses, 1x10^9 cells at days 0, 3, 7, 10;
Sacrifice day 14

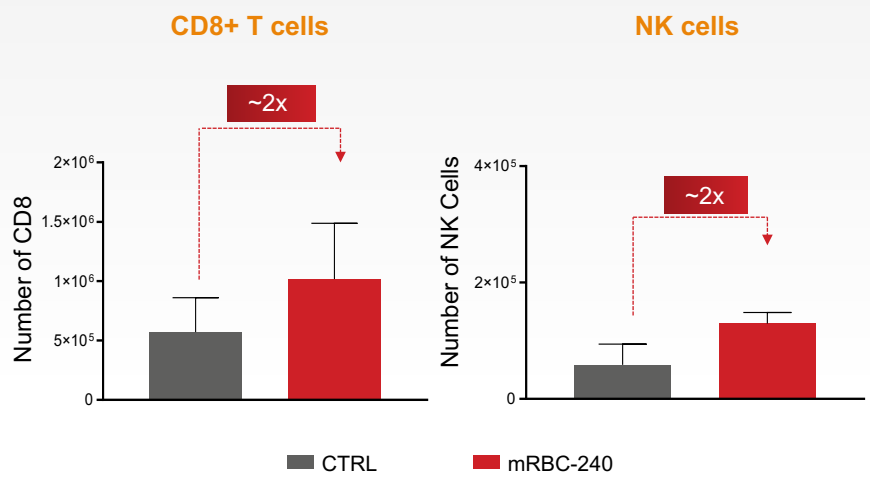
RTX-240 Preclinical Data Demonstrated Mechanism of Action In Vivo

T AND NK CELL EXPANSION IN BLOOD
(In Vivo with healthy mice)



Model details: Normal mice; 4 Doses, 1x10^9 cells at days 0, 3, 7, 10; Sacrifice day 14

T AND NK CELL TRAFFICKING TO TUMORS
(CT26 and B16F10 tumor models)

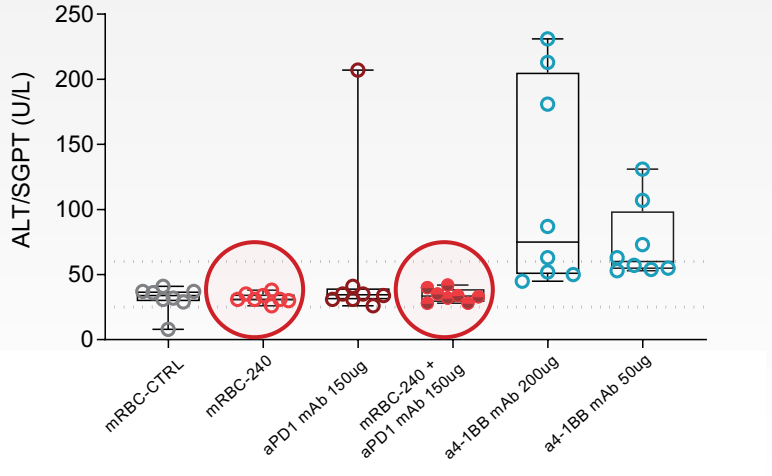


CT26 model details: 1x10^9 cells at days:1,5,8; PD evaluated in the tumors on Day 11

B16F10 model details: 1x10^9 cells at days:1,4,8; PD evaluated in the tumors on Day 10

mRBC-240 Resulted in No Liver Toxicity and Significantly Inhibited Tumor Growth as Monotherapy

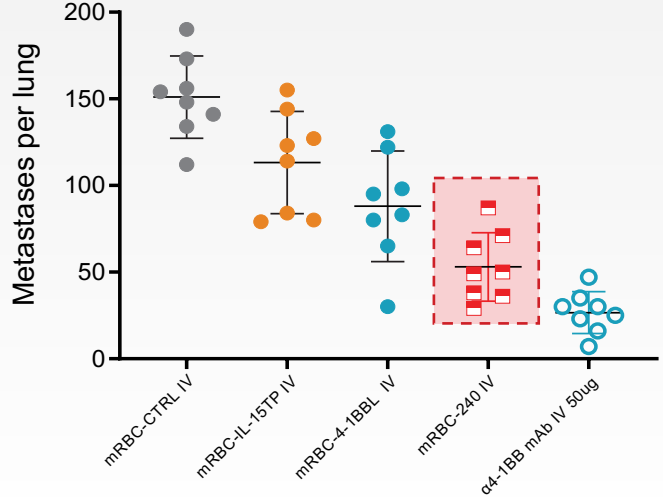
SERUM ALT



mRBC-240 showed no liver toxicity in vivo

4 Doses, $1x10^9$ cells day 0, 3, 7, 10; Sacrifice day 18

B16F10 LUNG METASTASES MODEL



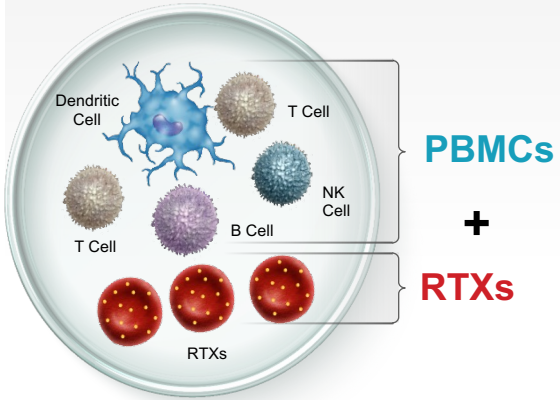
mRBC-240 reduced tumor burden and was equivalent to anti-4-1BB mAb in vivo

3 Doses, $1x10^9$ cells day 1, 5, 8, Sacrifice day 14

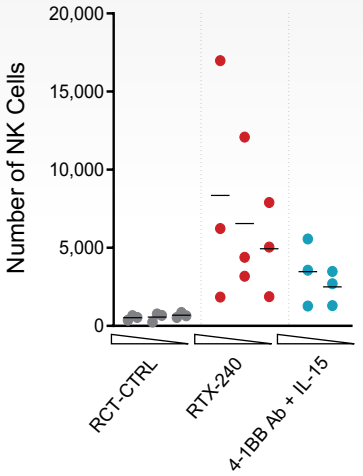
Dugast, et. al., *American Association for Cancer Research*; Poster #3272, 2019

RTX-240 Promotes Expansion and Activation of T and NK Cells In Vitro

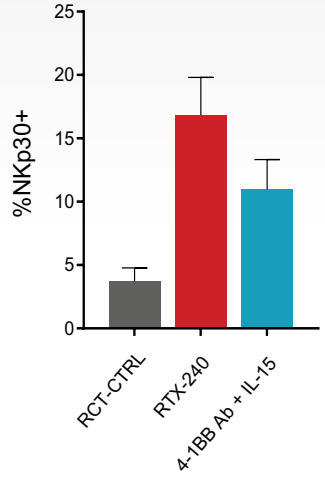
IN VITRO ASSAY



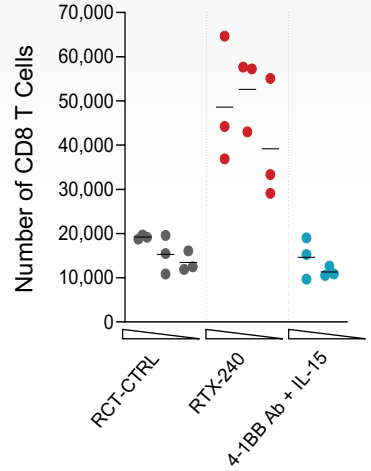
NK CELL NUMBER



PERCENT NKp30+ CELLS



CD8 CELL NUMBER



Dugast, et. al., *American Association for Cancer Research*; Poster #3272, 2019 and unpublished