

## **Delivering the Potential of Immunotherapy**

Corporate Overview April 2021

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## Legal Disclaimer



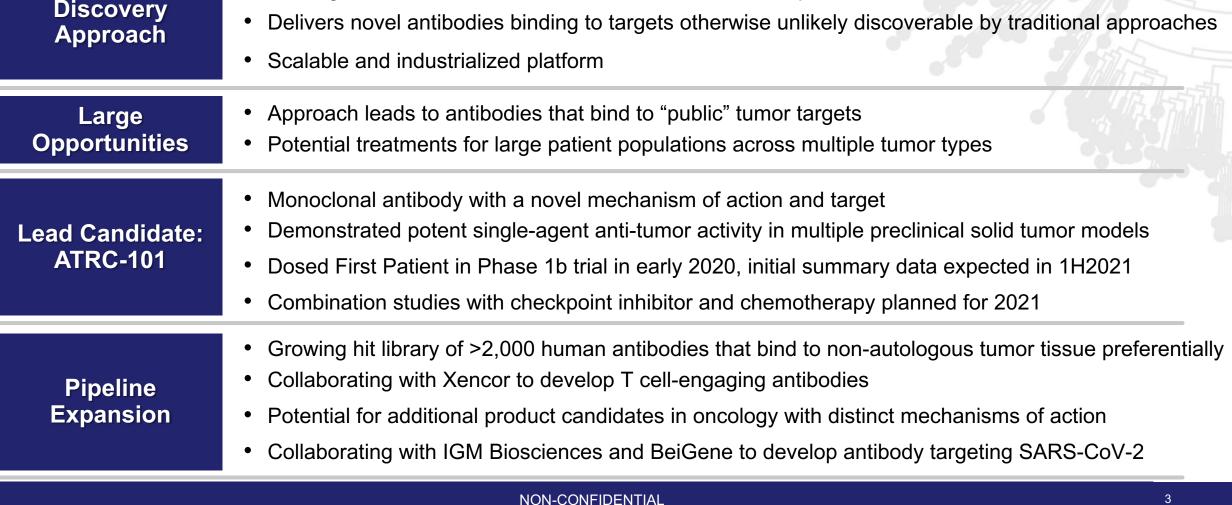
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You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this presentation and the accompanying oral commentary primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described in greater detail in our most recent Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission, and may cause our actual results, performance or achievement to differ materially and adversely from those anticipated or implied by our forward-looking statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this presentation. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

Moreover, we operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this presentation and the accompanying oral commentary. The results, events and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events or circumstances could differ materially from those described in the forward-looking statements.

This presentation discusses our current and potential future product candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these current or potential future product candidates for the use for which such product candidates are being studied.

The forward-looking statements made in this presentation and the accompanying oral commentary relate only to events as of the date on which the statements are made, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. We undertake no obligation to update any forward-looking statements made in this presentation and the accompanying oral commentary to reflect events or circumstances after the date of this presentation and the accompanying oral commentary or to reflect new information or the occurrence of unanticipated events, except as required by law. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments. We qualify all of our forward-looking statements by these cautionary statements.



First-mover advantages in accessing a potentially large and underexploited target space via

## **Company Highlights**

Differentiated

Discovering and Developing Novel Antibody-based Cancer Immunotherapeutics

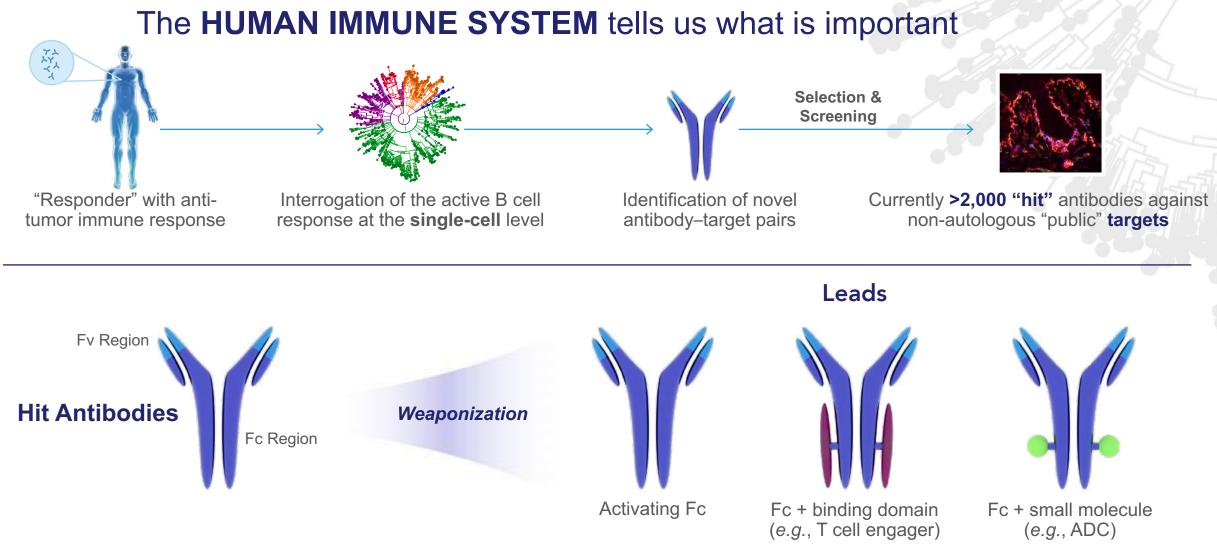
interrogation of the human active anti-tumor immune response



## The Atreca Discovery Platform

## Our Novel Approach Inverts the Discovery Paradigm

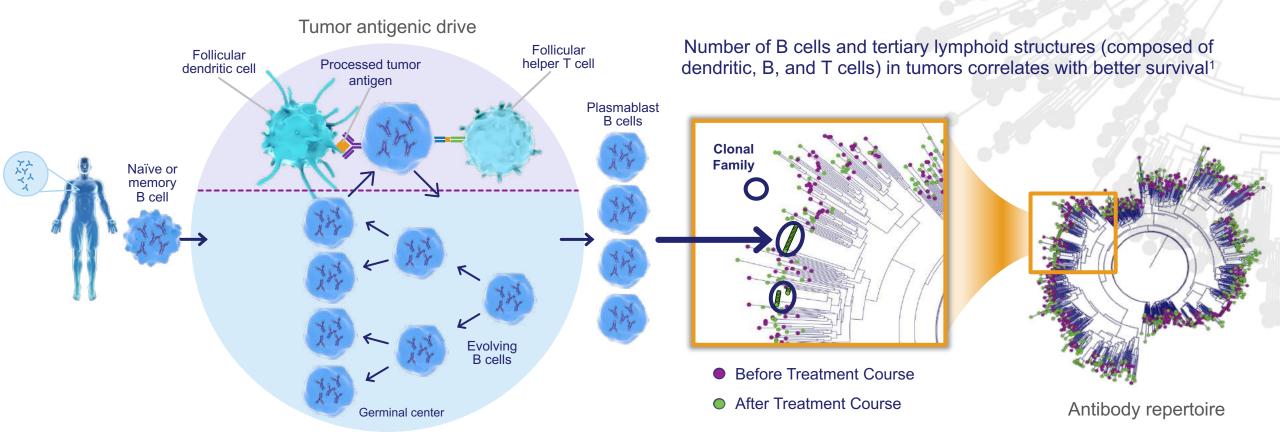




ADC, antibody-drug conjugate.

## B cells and Generation of Plasmablasts in Anti-Tumor Immune Responses



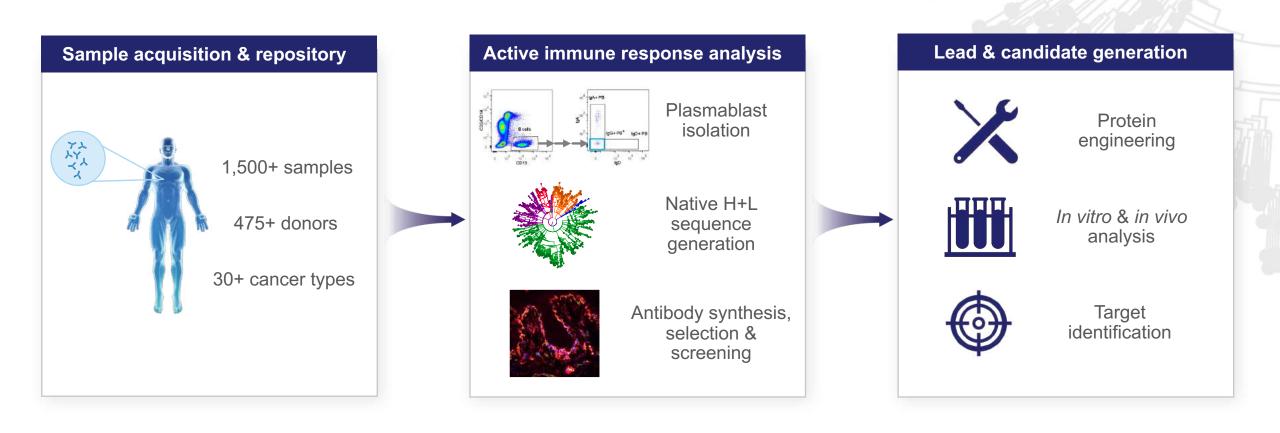


Analyses of plasmablasts generated in cancer patients indicate that these patients have an antigen-driven B cell response similar to those driven by antigens in infectious disease or autoimmunity<sup>2</sup>

1. Petitprez F, et al. Nature. 2020;577:556-560. 2. DeFalco J, et al. Clin Immunol. 2018;187:37-45.

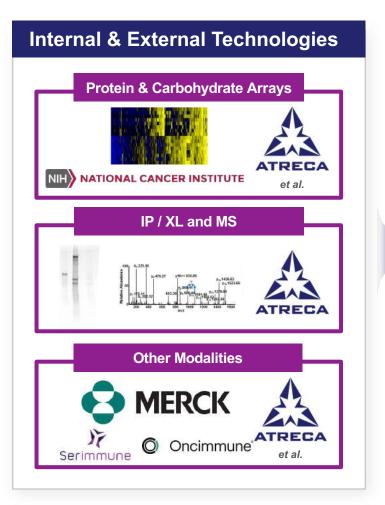


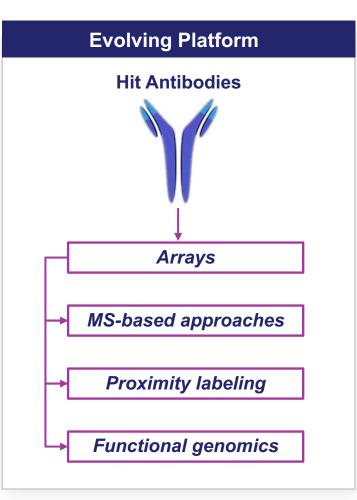
## Platform Provides Robust Industrialization Capabilities





## Expanded Target ID Platform Delivering



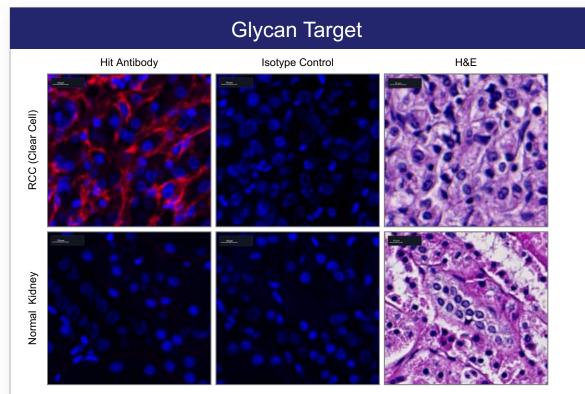


### **Accelerating Output Array screening** Initial step 100's of antibodies per year • > 25% of input antibodies positive **Targets confirmed in 2020** 13 confirmed from 75 array positives Targets ID'ed in multiple classes • Transmembrane proteins Glycans • • RNA-binding proteins Et al. •

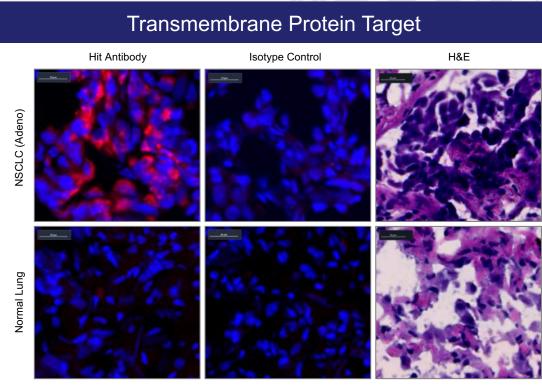
MS, mass spectrometry.



## **Examples of Antibody-Target Pairs**



- Novel oncology target
- Present in multiple tumor types
- Active in ADCC, ADCP assays
- Being evaluated in multiple potential formats



- Known oncology target (no approved therapy)
- Present in multiple tumor types
- Active in ADCC, ADCP, ADC assays
- Being evaluated in multiple potential formats

ADCC, antibody-dependent cellular cytotoxicity; ADCP, Antibody-Dependent Cellular Phagocytosis; ADC, antibody-drug conjugate.

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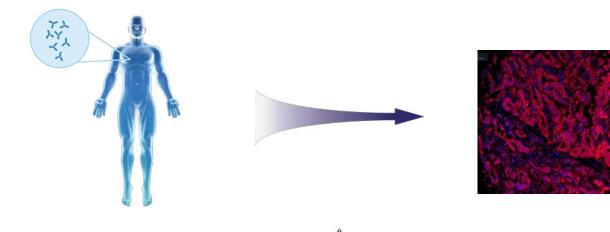


## **ATRC-101**



## ATRC-101: A New Way to Target Cancer

### Engineered version of a patient antibody discovered via the Atreca platform



Lung adenocarcinoma patient with active anti-tumor immune response

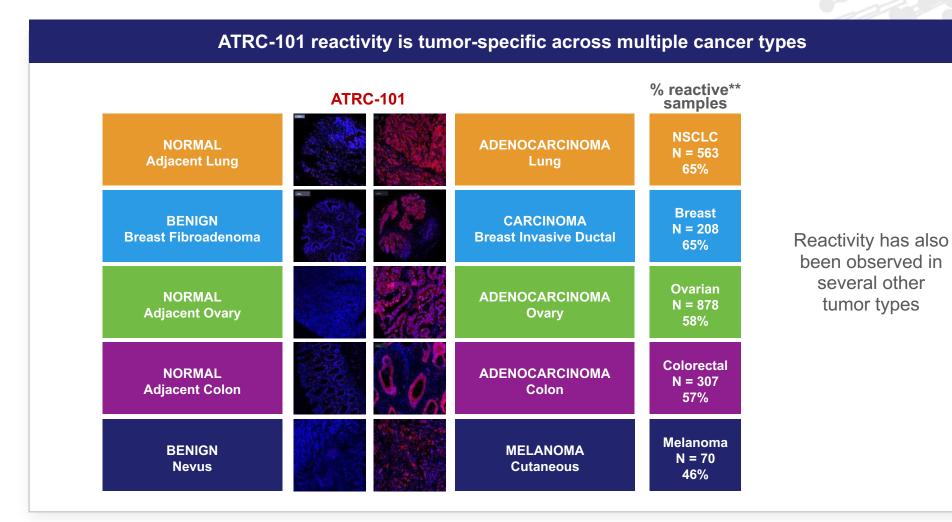


ATRC-101 binds its target in multiple tumor types from different patients

- First-in-class program
  - Novel target
  - Novel MOA
- Phase 1b trial in dose escalation stage enrolling patients with solid tumors
  - NSCLC
  - Breast
  - Ovarian
  - Colorectal
  - Acral melanoma
- Plans for combination trials with checkpoint inhibitors and with chemotherapy



## ATRC-101 Has Potential to Treat Large Groups of Patients



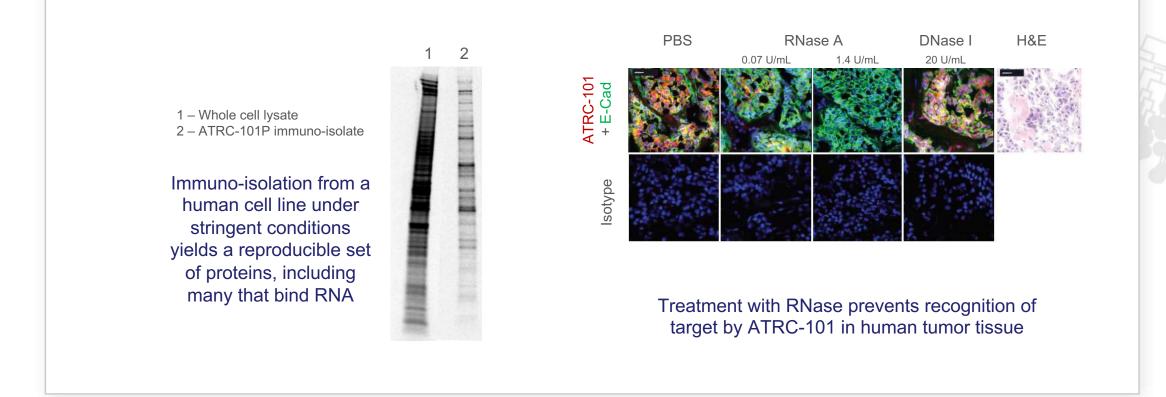
\*\* "Reactive" samples had moderate to high signal overall with ≥40% malignant cells positive (N = total samples). Samples were largely from treatment-naïve patients. Percentages based on samples from all subtypes within solid tumor type

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## ATRC-101 Targets a Ribonucleoprotein Complex

Isolated target of ATRC-101 is composed of multiple RNA-binding proteins and RNA



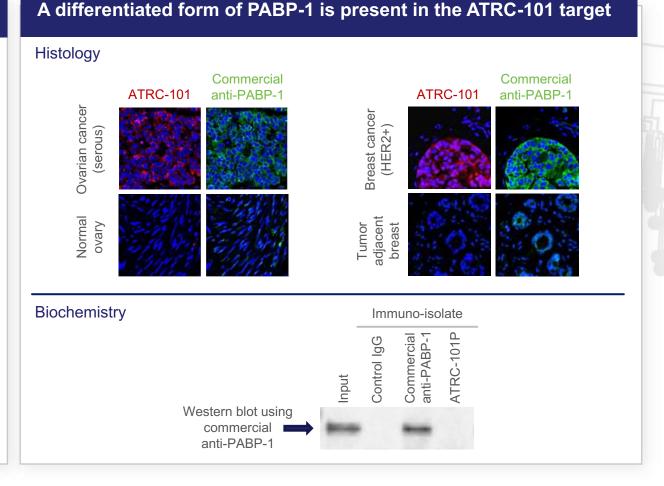
## ATRC-101 Binds an RNP Complex with Polyadenylate-Binding Protein (PABP) Family Members



# PABP-1 bound to mRNA forms an abundant complex Polyadenylate-binding protein (e.g., PABP-1) bound to mRNA<sup>1</sup>

PABP-1 is a highly abundant protein in normal cells that binds to almost all mRNAs and plays a vital role in mRNA biology via facilitating protein–protein interactions<sup>2,3</sup>

We believe that the key property of PABP-1 important for ATRC-101 activity is its ability to bind almost all mRNA species

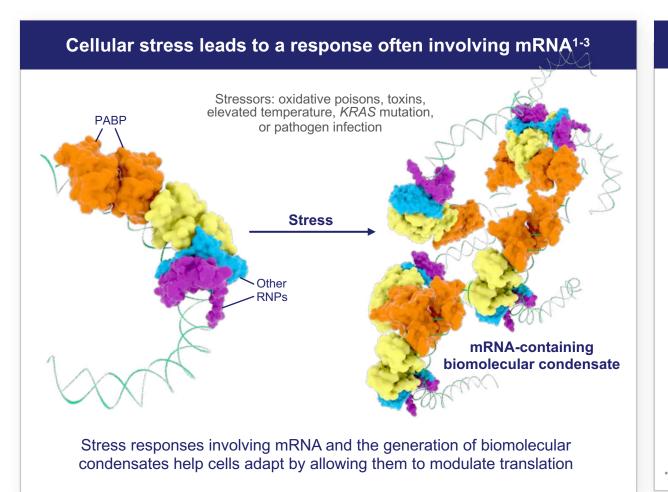


1. Schafer IB, et al. Cell. 2019;177:1619-1631. 2. Goss DJ, et al. WIREs RNA. 2013;4:167-179. 3. Gorlach M, et al. Exp Cell Res. 1994;211:400-407.

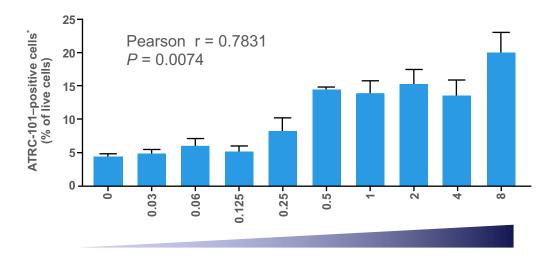
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## Stress Induces the Target of ATRC-101 in Tumor Cells



### Stress induces the target of ATRC-101



NaAsO<sub>2</sub> concentration [mM]

Stress induction of the target of ATRC-101 together with the biochemical properties and composition of the immuno-isolated target indicate that the target RNP complex has the hallmarks of a biomolecular condensate

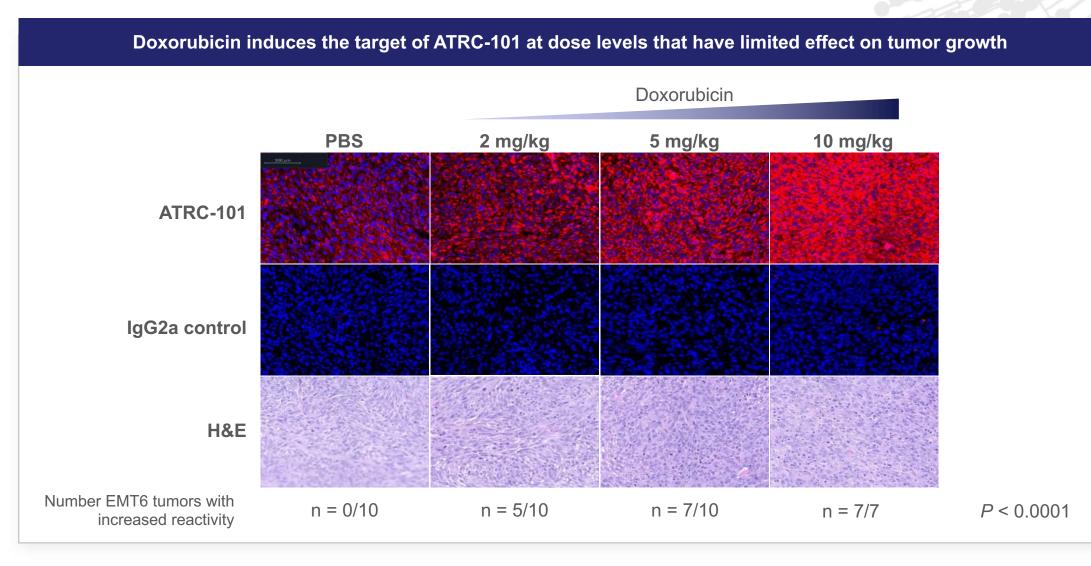
\* Error bars based on the standard error of technical replicates

G3BP, Ras-GAP SH3 domain binding protein; mRNA, messenger RNA; NaAsO<sub>2</sub>, sodium arsenite; PABP, polyadenylate-binding protein; RNP, ribonucleoprotein. 1. Tourriere H, et al. *J Cell Biol*. 2003;160:823-831. 2. Protter DSW, et al. *Trends Cell Biol*. 2016;26:668-679. 3. Guillen-Boixet, J, et al. *Cell*. 2020;181:346-361.

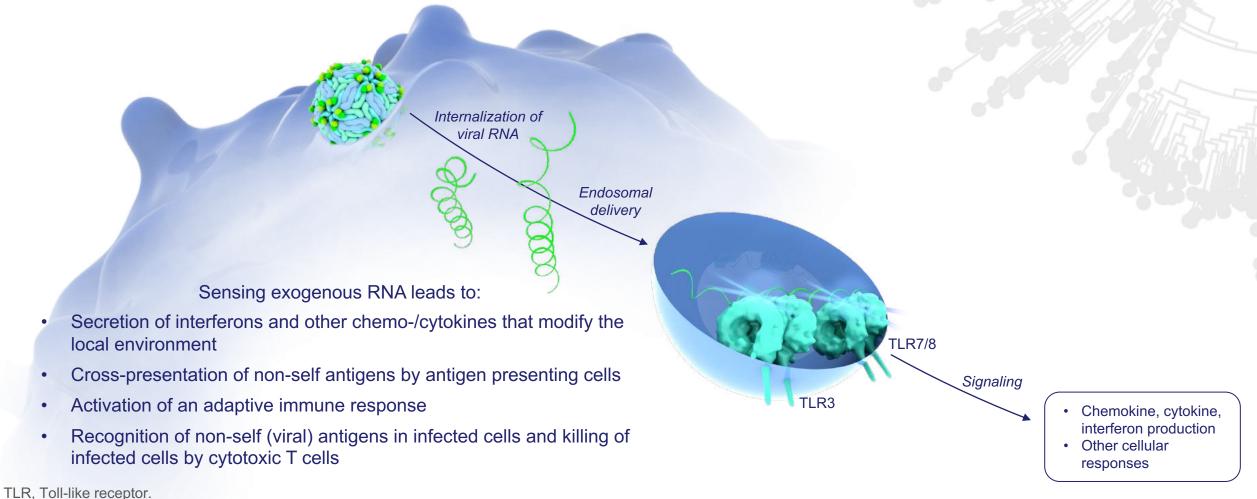
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## Chemotherapy Induces Target of ATRC-101 in vivo



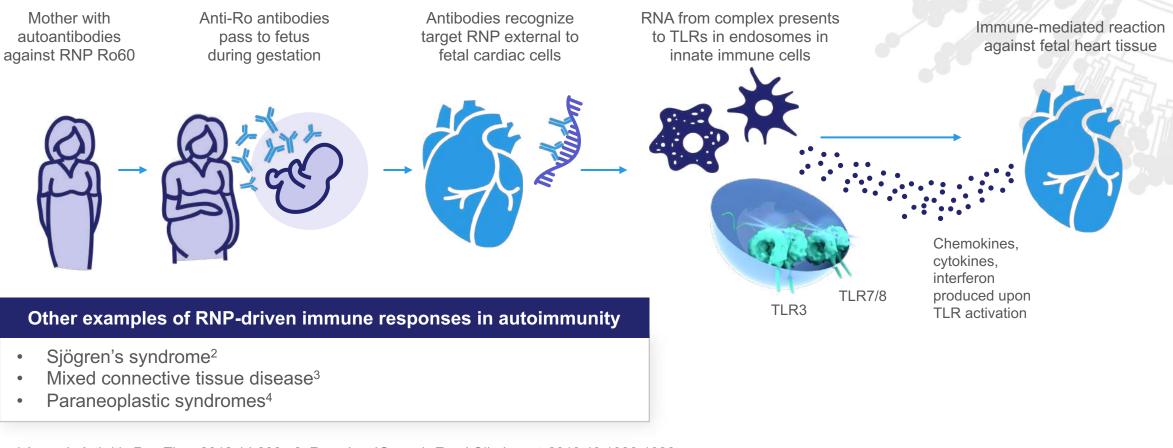
### Detection of Exogenous RNA by Myeloid Cells is Important in Immune Responses Against Viral Infection



## RNP Complexes are Antigens that Drive Tissue-Destructive Immune Responses in Autoimmune Disease



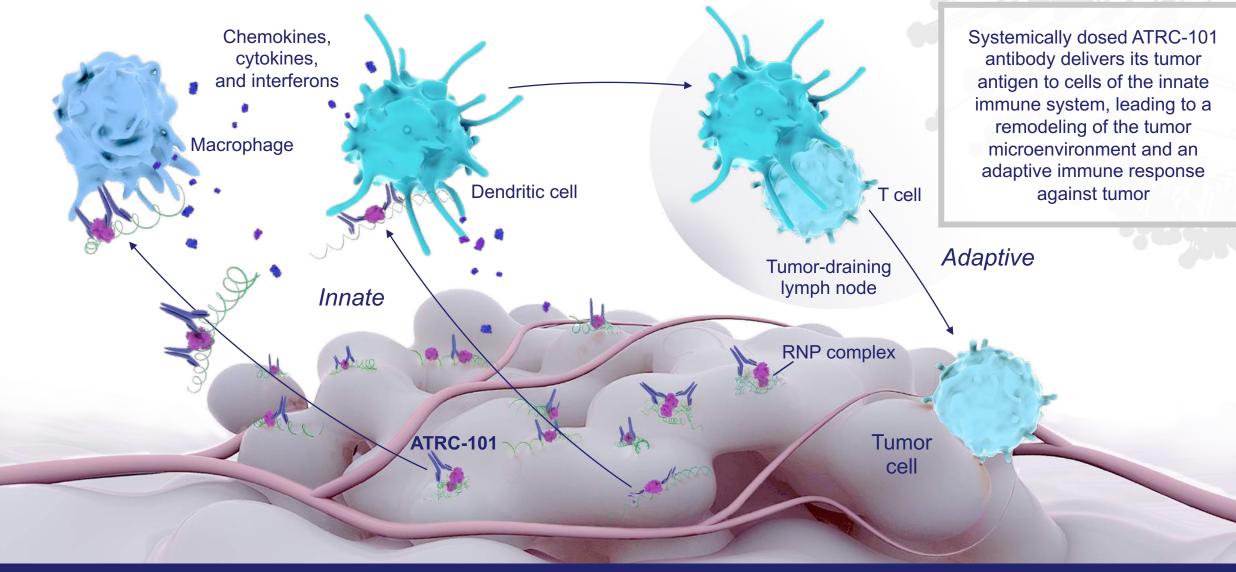
### Neonatal lupus as an example of immune response initiated by an antibody-RNP complex in humans<sup>1</sup>



1. Ambrosi A, et al. *Arthritis Res Ther*. 2012;14:208. 2. Routsias JG, et al. *Eur J Clin Invest*. 2010;40:1026-1036. 3. Agris PF, et al. *Immunol Commun*. 1984;13:137-149. 4. Darnell RB, et al. *N Engl J Med*. 2003;349:1543-1554.

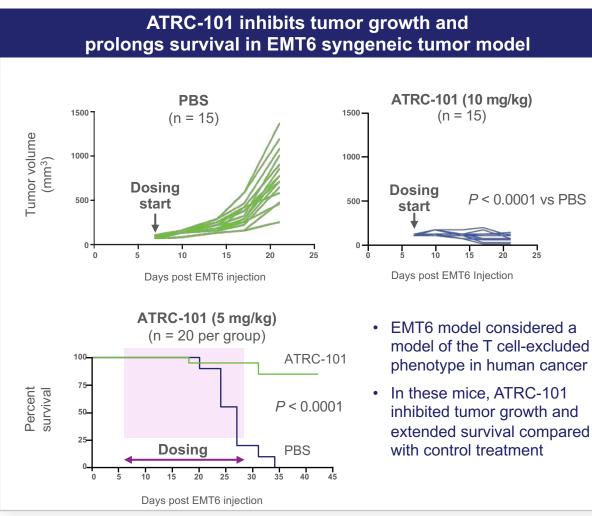


## ATRC-101: A Novel Way to Target Cancer

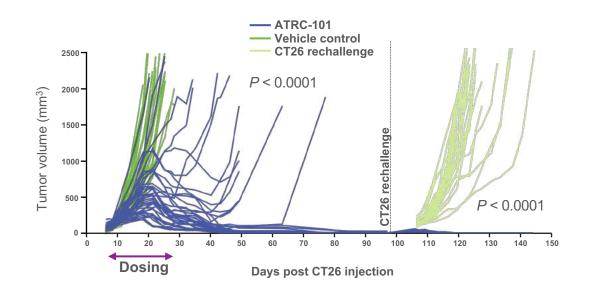


## ATRC-101 Exhibits Potent Single-Agent Activity in Mouse Models of Cancer





ATRC-101 inhibits tumor growth and leads to immune memory in CT26 syngeneic model



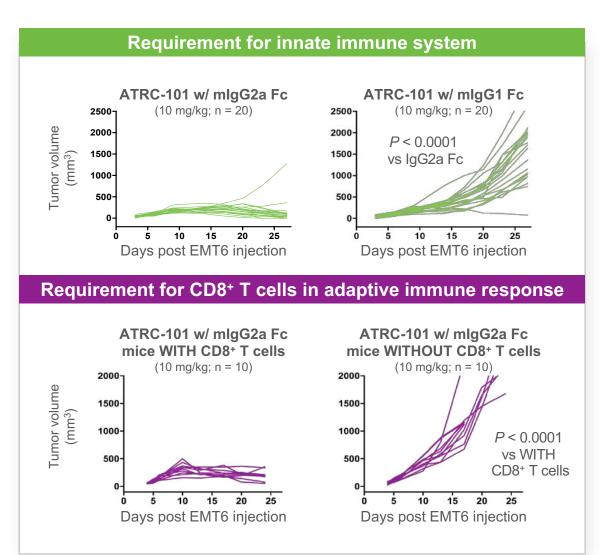
Large tumors can be eradicated in this model by continued dosing with ATRC-101

Immune memory prevents re-establishment of tumors after tumor clearance by a second CT26 injection (also observed in EMT6 model)

PBS, phosphate buffered saline.

## ATRC-101 Activity Requires both Innate and Adaptive Immune Responses



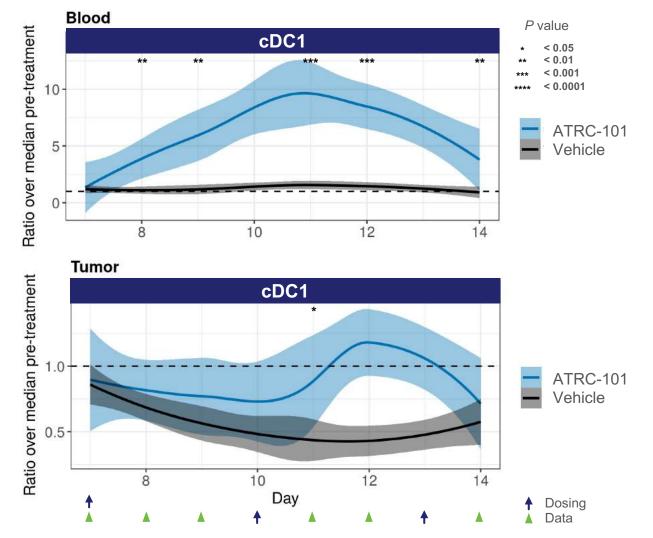


- NK cells or complement-dependent cytotoxicity alone cannot drive activity, as activity is lost in *nu / nu* mice
- Overall, these and other data indicate that activity *in vivo* requires:
  - ATRC-101 Fc to bind to FcRs on innate immune (likely myeloid) cells
  - Induction of cytotoxic CD8<sup>+</sup> T cell response

FcR, Fc receptor; NK, natural killer.

## ATRC-101 Changes the Immune Cell Profile of the Tumor Microenvironment and Blood in Animal Models



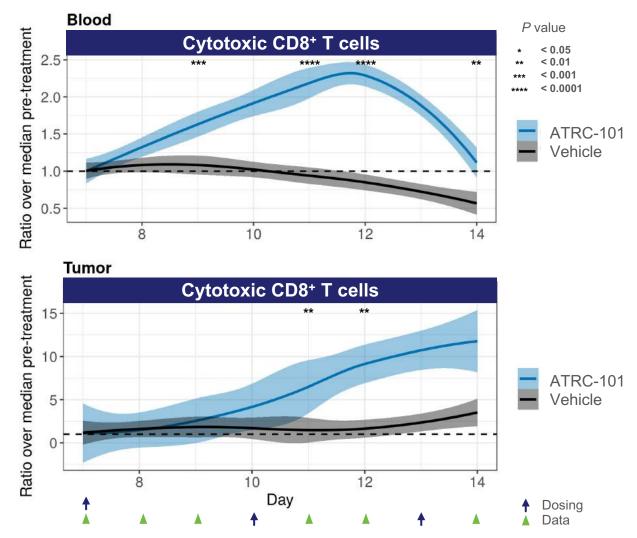


- cDC1 dendritic cells: Myeloid cell type that transports antigens to lymph nodes and cross-presents those antigens in class I MHC, leading to activation of cytotoxic T cells
- Effects of ATRC-101 on number of cDC1s in blood are almost immediate (within 24 hours), consistent with their activation in tumor and trafficking to lymph nodes

cDC1, conventional dendritic cell subtype 1; MHC, major histocompatibility complex.

## ATRC-101 Changes the Immune Cell Profile of the Tumor Microenvironment and Blood in Animal Models

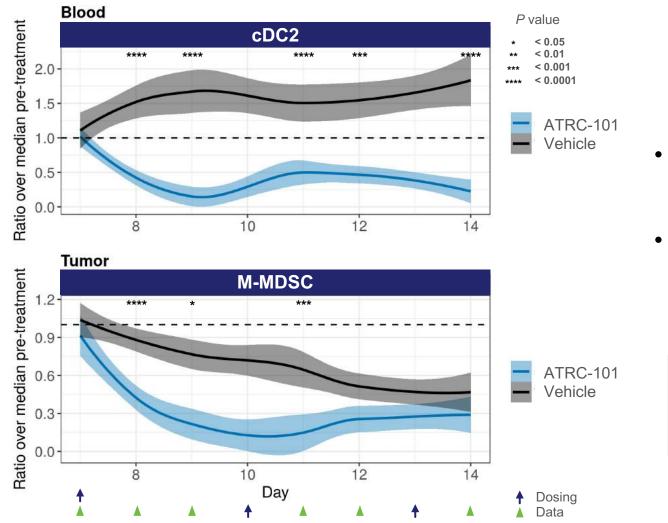




- Cytotoxic CD8<sup>+</sup> T cells also start increasing in blood with only a slight delay relative to cDC1 cells
- CD8<sup>+</sup> T cells then start appearing in the tumor in significant numbers after a delay, consistent with their activation in and trafficking from lymph nodes

## ATRC-101 Changes the Immune Cell Profile of the Tumor Microenvironment and Blood in Animal Models



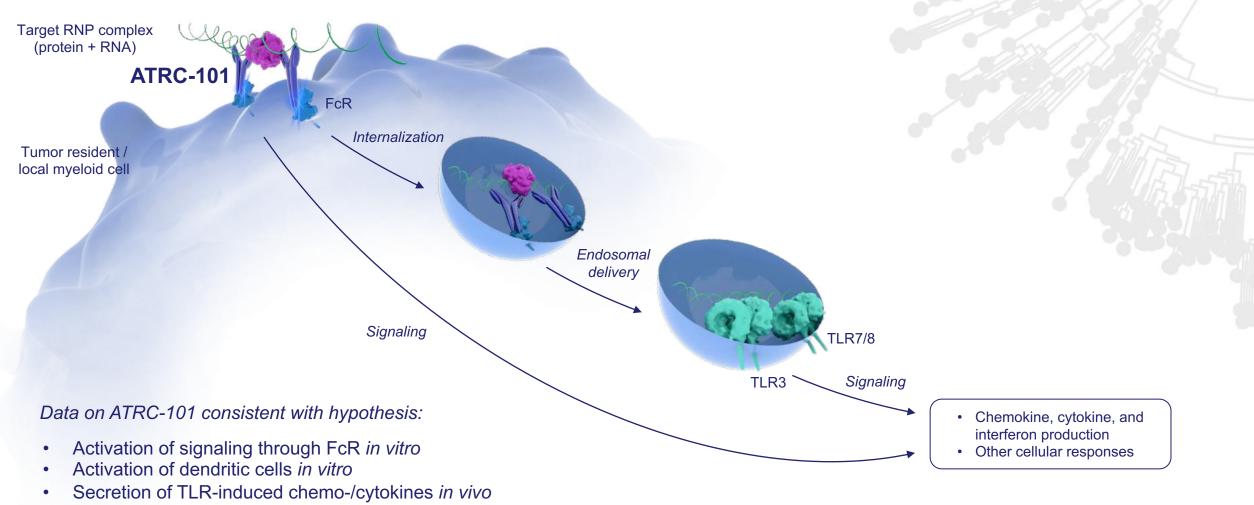


- Contrasting with cDC1 cells, numbers of cDC2 dendritic cells in the blood decrease almost immediately with ATRC-101 dosing
- Within the tumor, numbers of immune-suppressive M-MDSC cells also drop almost immediately with ATRC-101 dosing

ATRC-101 treatment also induces macrophage polarization toward the M1 and away from the M2 phenotype

cDC2, conventional dendritic cell subtype 2; M-MDSC, monocytic myeloid-derived suppressor cell; TME, tumor microenvironment.

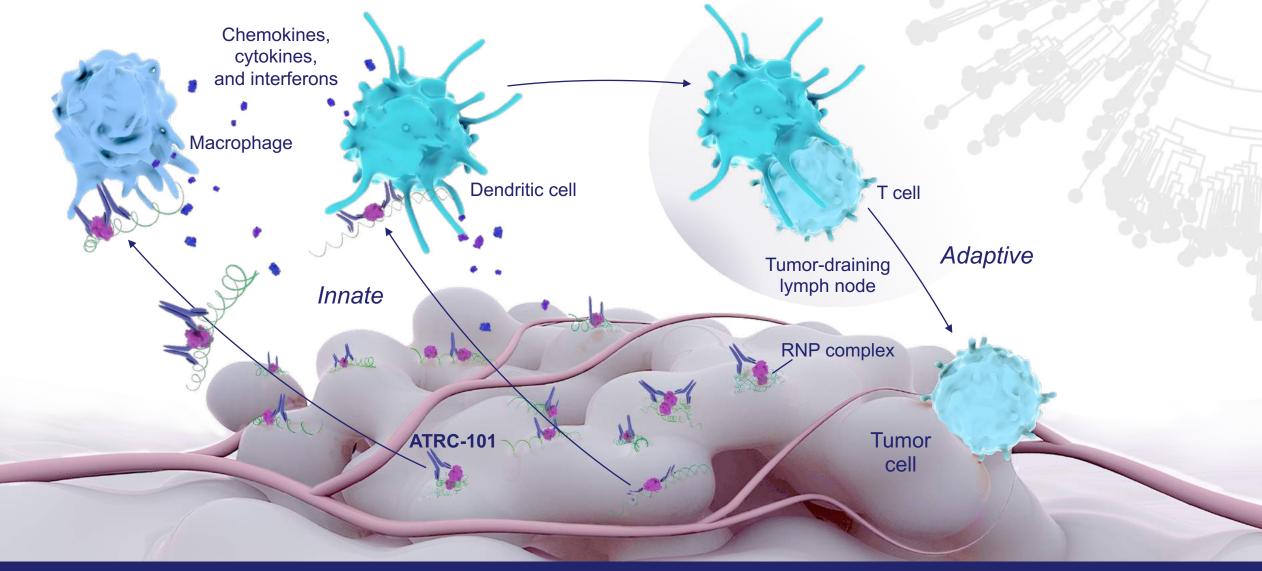
## Hypothesis: Dual FcR and TLR Activation Delivers Activity



• Expression of interferon-stimulated genes in vivo

## ATRC-101 Engages an RNP-Driver Antigen that Elicits Both Innate and Adaptive Immune Responses

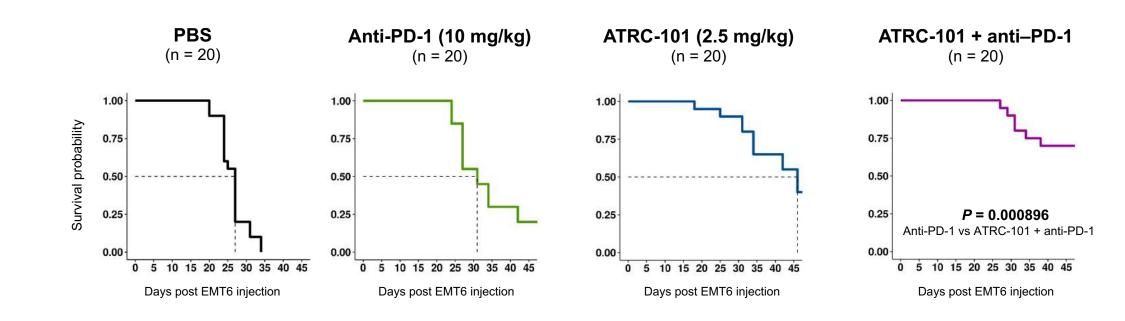




ATRC-101 Facilitated Activity of Checkpoint Inhibitors and other T Cell Focused Therapeutics in an Animal Model



ATRC-101 facilitates anti-PD-1 activity in a model of the T cell-excluded phenotype



Anti-PD-1: Dosing 2x per week x 2 weeks (last dose Day 21). ATRC-101 antibody: Dosing 2x per week x 3.5 weeks (last dose Day 28).

By engaging the innate immune system to modify the tumor microenvironment and drive an adaptive immune response involving T cells, ATRC-101 may lead to greater activity for agents that target T cells

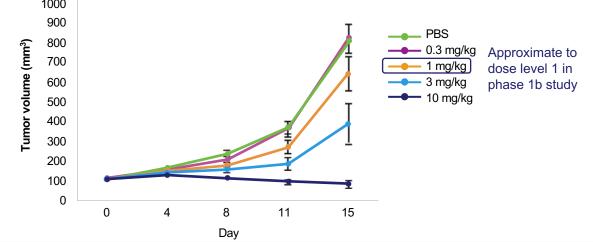
## ATRC-101 Possesses Dose-Dependent Activity in Preclinical Models with No Substantial Safety Concerns



## Dose-dependent tumor growth inhibition and activity

### Phase 1b dosing

- Correlation between dose and anti-tumor activity demonstrated in preclinical studies
- Starting dose in the phase 1b trial (0.3 mg/kg) approximates the 1 mg/kg dose evaluated in the EMT6 mouse model



### Safety studies summary

### Normal tissue binding

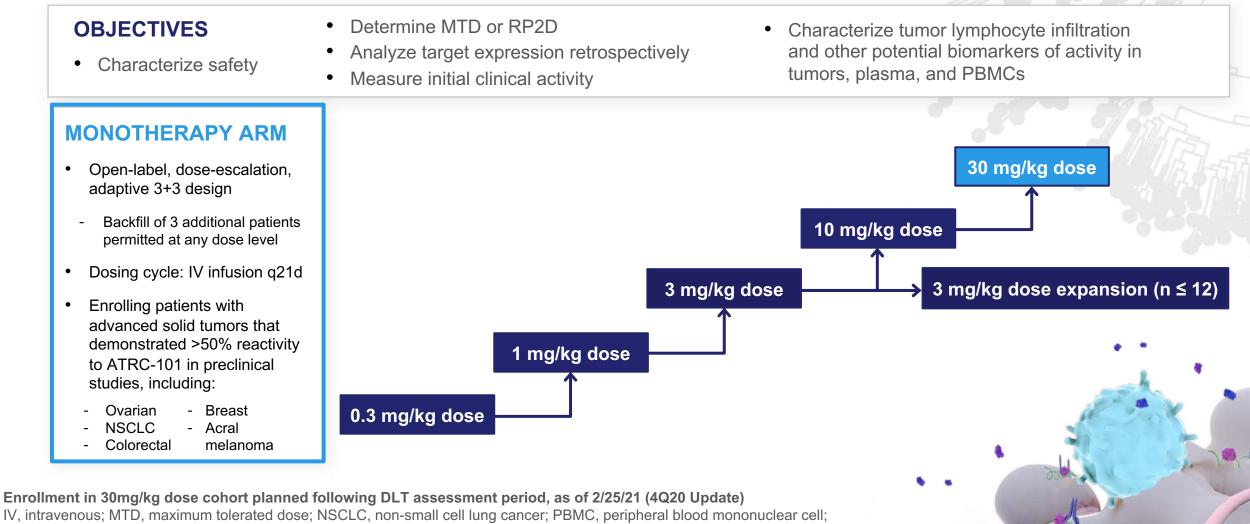
 No signal of toxicological significance observed across a wide range of normal human tissues in a GLP tissue cross-reactivity study

### In vivo safety assessments

- Four repeat doses over 4 weeks of up to 100 mg/kg in NHPs were well tolerated and no definitive safety signals were observed
- No definitive safety signals observed in repeat dose safety studies in normal and tumor-bearing mice (EMT6)



## A Phase 1b Trial was Initiated in Early 2020



q21d, every 21 days; RP2D, recommended phase 2 dose; DLT, dose-limiting toxicity.



## **Considerations For Clinical Development**

### Monotherapy (enrolling)

### Rationale

 Monotherapy activity in preclinical models

### **Trial stages\***

- Dose-escalation/expansion to characterize safety and identify RP2D
  - Eligibility multiple tumor types defined by target expression
- Efficacy expansion cohorts (single indication or biomarker defined)

### **Checkpoint inhibitor combination**

### Rationale

- Supported by MOA
- Preclinical data suggestive of synergy

### **Trial stages\***

- Dose escalation with fixed dose of checkpoint inhibitor
- Efficacy expansion/phase 2

### **Chemotherapy combination**

### Rationale

- Chemo may increase target expression
- Chemo may promote antigen release
- Independent pathways to cell killing
- Precedence of combining chemotherapy with tumor-targeting antibodies (*e.g.*, trastuzumab plus paclitaxel)
- Opportunity to introduce earlier in treatment course

### **Trial stages\***

 Phase 2 with safety run-in at dose level RP2D-1

\* Trial stages and study designs are subject to FDA agreement and emerging data.

Chemo, chemotherapy; FDA, United States Food and Drug Administration; MOA, mechanism of action; RP2D, recommended phase 2 dose.

## Pipeline

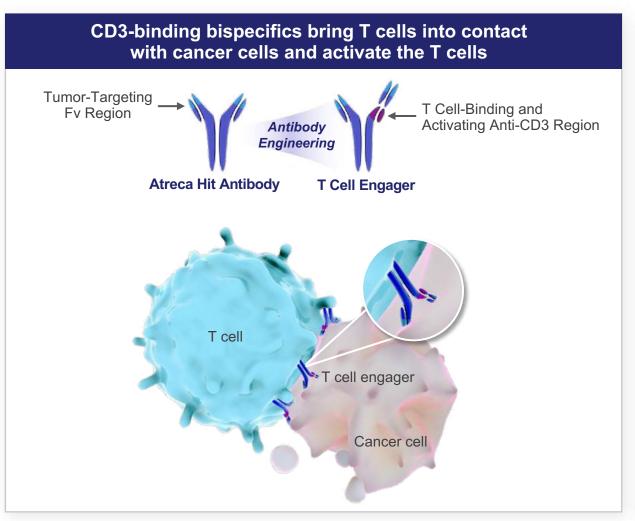
## Pipeline

ONCOLOGY		Asset (Target)	MOA	Discovery / Preclinical	Phase 1	Phase 2	Collaborators
Activating Fc	Y	ATRC-101 (Novel RNP Complex)	Driver Antigen Engagement				ATRECA
Fc + binding domain	Ì	Multiple	T Cell Engagement				ATRECA SXencor
		Multiple	Multiple (e. <i>g.,</i> NK Cell-Targeted and Others)				ATRECA
Fc + small molecule		Multiple	ADC (Cytotoxic)				+ undisclosed
		Multiple	Immunostimulation				+ undisclosed
COVID-19							
Alliance to discover, develop, and manufacture therapeutic antibodies		Multiple	Targeting SARS-CoV-2				

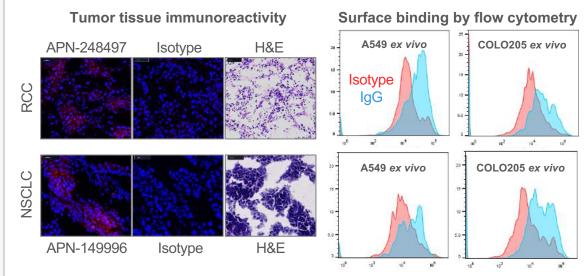
ADC, antibody–drug conjugate; MOA, mechanism of action; NK, natural killer.

### T Cell Engagers Xencor Partnership





### Atreca antibodies being advanced as T cell engagers have been characterized *in vitro*



- Atreca antibodies have also been characterized for:
  - Reactivity to other tumor types and normal tissues
  - Expression, thermal stability, and polyspecificity in multiple Xencor bispecific formats
  - T cell-dependent cellular cytotoxicity in bispecific format

CD3, cluster of differentiation 3; H&E, hematoxylin and eosin; IgG, immunoglobulin; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma.

## Collaborating with Xencor to Discover and Develop Novel T Cell-Engaging Bispecific Antibodies



- Atreca will provide antibodies against novel targets from which Xencor will engineer XmAb bispecific antibodies that bind to the CD3 receptor on T cells
- Up to two joint programs will be mutually selected for further development and commercialization with 50/50 cost and profit sharing
  - Each company will lead development, regulatory, and commercialization activities for one of the joint programs
  - Atreca to lead the first joint program
- Each partner may pursue up to two programs independently with royalties payable on net sales; **Xencor** to select and lead the first independent program
- Work began in 2019 under a material transfer agreement to accelerate the collaboration
- Xencor is a leader in generating CD3-binding bispecific T cell engagers from initial antibody engineering and manufacturing through clinical development; advantages of the platform relevant to Atreca include:
  - Bispecific Fc domain technology that retains full-length antibody properties in a bispecific antibody format
  - Ability to tune the potency of T cell killing in a plug-and-play manner



## Alliance to Discover, Develop, and Manufacture Potential Antibodies Targeting SARS-CoV-2 to Treat COVID-19







- Discovery platform has a track record of generating potent, neutralizing antibodies in infectious disease
- Focus on plasmablast B cells may lead to antibodies against
  epitopes missed by bait-based approaches focused on spike protein
- IgM and IgA antibodies produce better binding, cross-reactivity, neutralization, and mucosal transport vs traditional IgG antibodies
- Platform enables the rapid development and production of engineered therapeutics

### Alliance announced in April 2020

- Alliance will leverage the differentiated technology, expertise, and infrastructure of each party
- Due to urgency of the pandemic, parties began work immediately and will finalize financial details and other terms in the future
- Clinical candidate may be ready for human testing in 1H2021

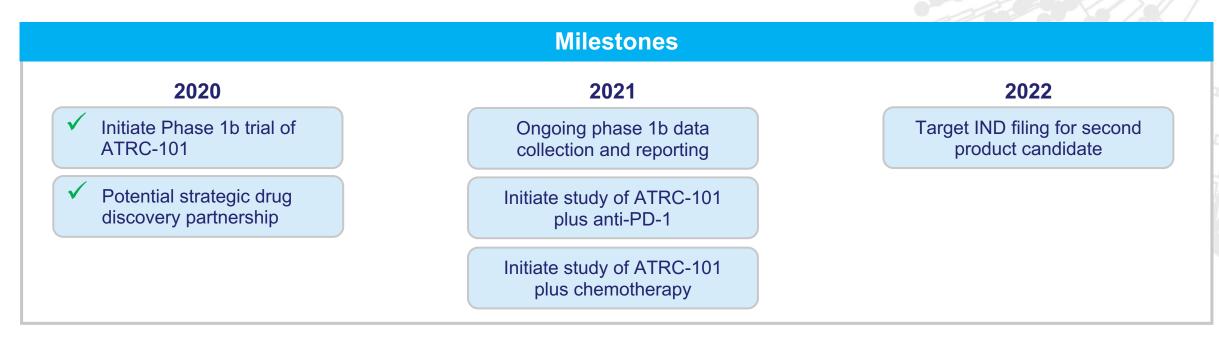


1,100-person global development and regulatory team across China, the United States, Europe, and Australia

## **Key Milestones and Financial Overview**



## Anticipated Milestones and Financial/IP Overview

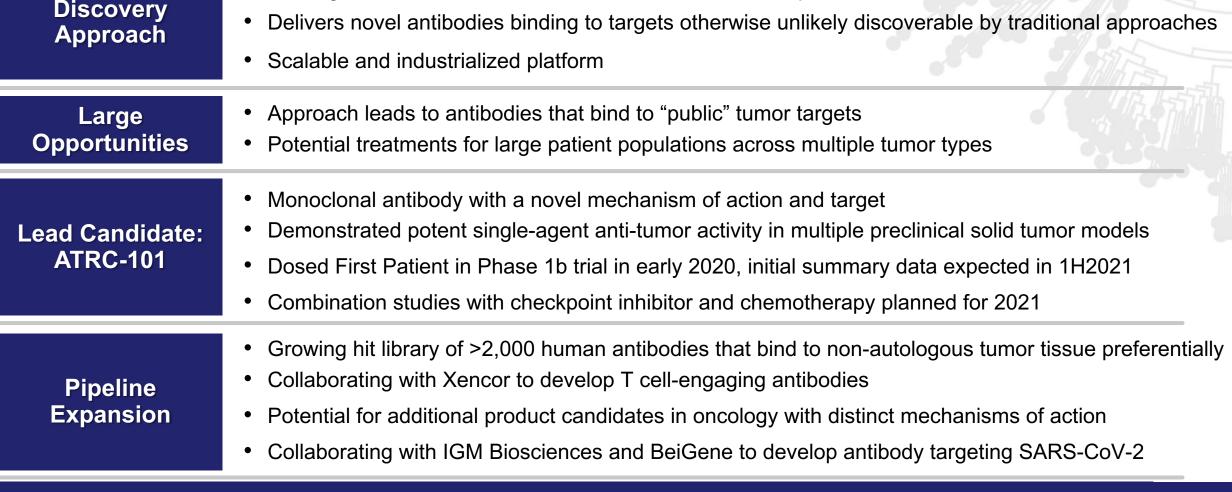


### **Financial Overview**

- **\$125M** equity financing completed in **July 2020**
- Current capital expected to be adequate to fund operations into 1H23
- Cash, cash equivalents & investments of \$240.1M as of December 31, 2020

### Intellectual Property

- Patents issued in multiple jurisdictions covering key aspects of Atreca technologies and platform
- Patent applications covering compositions of matter and methods of use for ATRC-101 and related antibodies filed internationally



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First-mover advantages in accessing a potentially large and underexploited target space via

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Discovering and Developing Novel Antibody-based Cancer Immunotherapeutics

interrogation of the human active anti-tumor immune response

