NON-CONFIDENTIAL PROPRIETARY PRESENTATION



### 2022 R&D Day

April 5, 2022

### Legal Disclaimer



This presentation and the accompanying oral commentary contain forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation and the accompanying oral commentary, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements because they contain words such as "potential," "believe," "target," will," "demonstrate," "expect," "anticipate," "continue," "may," "plan," "predict," "present," "aim," "goal" or the negative of these words or other similar terms or expressions, although not all forward-looking statements contain these words. These forward-looking statements include, but are not limited to, statements concerning the following: the initiation, timing, progress and results of our research and development programs, preclinical studies, and clinical trials; our strategy and future plans, including our Phase 1b trial of ATRC-101 and statements regarding the development of ATRC-101 and our preclinical, clinical, and regulatory plans, and the timing thereof; the availability and timing of data from monotherapy dose expansion cohorts in our Phase 1b trial of ATRC-101 and from combination cohorts evaluating ATRC-101 with pembrolizumab and with and other data readouts; plans to begin participant selection based on target expression; our ability to identify potentially valuable therapeutic antibodies through our discovery platform and collaborations with third-parties; our ability to weaponize or otherwise optimize our lead antibodies; our plans for utilizing ZymeLinkTM technology with the agreement with Zymeworks; our plans to utilize the ZymeLinkTM platform in connection with ATRC-301; the development of ATRC-301 and our preclinical and clinical plans, specifically, plans to present results of IND-enabling studies for ATRC-301 in the second half of 2022 and our ability to submit an IND application for ATRC-301 in the second half of 2023, including the timing thereof; our plans regarding a first in human study of ATRC-301 in the first half of 2024; the safety and potential efficacy of our clinical candidates, including ATRC-301, ATRC-101 and our anti-SARS-CoV-2 antibody discoveries; our ongoing evaluation, optimization and expansion of our pipeline of oncology programs, including ADC leads APN-497444 and APN-959038, CD3-engager lead APN-346958, and IL-15 SA conjugate lead APN-541885, and the productivity of such programs; our ability to continue to develop new clinical candidates for IND applications and our ability to submit one such application per year; plans to present new information on our EphA2 program and other pipeline antibodies; plans regarding the evaluation of clinical data; our enrollment objectives; our ability to obtain sufficient clinical enrollment; reports of clinical enrollment updates; our ability to fund current operations and develop and commercialize our current or potential future product candidates; our ability to identify and develop product candidates for treatment of additional disease indications; our expectations regarding the achievement and timing of research, development, clinical, regulatory and other corporate milestones; our anticipated milestones and the implementation of our business model and strategic plans for our business, technologies, and current or potential future product candidates; and the ability to obtain intellectual property rights for our current and potential future product candidates. 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 filings with the Securities and Exchange Commission (SEC) and available on the SEC's website at www.sec.gov, including in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of our most recently filed Annual Report on Form 10-K, and may cause our actual results, performance or achievement to differ materially and adversely from those anticipated or implied by our forward-looking statements. 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. 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 plans, expectations, 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. 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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments. We qualify all our forward-looking statements by these cautionary 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.

## Today's speakers



John Orwin President and CEO



Amy Manning-Bog, PhD VP, Translational Sciences

Tito Serafini, PhD Chief Strategy Officer



**Shaun Lippow, PhD** VP, Protein Engineering

Daniel Emerling, PhD SVP, Research



Alexander Scholz, PhD Senior Director, *In Vitro* Pharmacology

## Available for questions

Jonathan Benjamin, MD PhD SVP, Clinical Research

Herb Cross Chief Financial Officer





### Agenda

- Introduction Tito Serafini, PhD
- **Discovery Platform** Daniel Emerling, PhD
- Anti-EphA2 Program and Clinical Candidate
  - Amy Manning-Bog, PhD / Shaun Lippow, PhD / Alexander Scholz, PhD

#### • Lead-Stage Programs

- ADCs and the Atreca ADC Engine Alexander Scholz, PhD
- Tumor-targeting CD3 T Cell Engager Shaun Lippow, PhD
- Tumor-targeting IL-15SA Fusion Amy Manning-Bog, PhD
- Summary and Upcoming Milestones John Orwin
- Q&A

### **Executive Summary**



Platform	<ul> <li>Atreca's drug discovery approach and platform validated by ATRC-101 clinical data</li> <li>Atreca platform continues to evolve and is delivering a robust pipeline</li> </ul>
ATRC-301	<ul> <li>Antibody Drug Conjugate (ADC) targeting EphA2 declared as clinical candidate</li> <li>Enabled by newly announced licensing agreement with Zymeworks</li> <li>Demonstrates potent anti-tumor activity <i>in vivo</i></li> <li>Differentiated from previous and current clinical-stage programs</li> </ul>
Pipeline	<ul> <li>Four additional lead-stage oncology programs advancing</li> <li>Lead antibodies bind novel tumor targets that vary in molecular class</li> <li>All programs have positive <i>in vivo</i> data</li> </ul>

ADC, antibody–drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2.

### Our Novel Approach Inverts the Discovery Paradigm



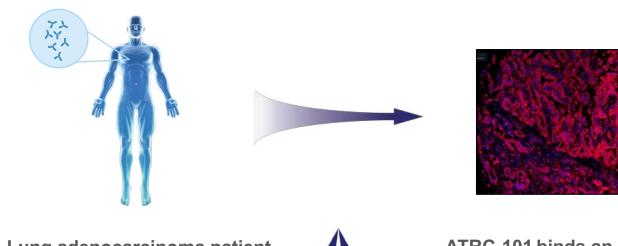
#### The HUMAN IMMUNE SYSTEM tells us what is important Selection & Screening Patient with anti-tumor Interrogation of the active B cell Identification of novel Currently >2,000 "hit" antibodies against response at the single-cell level non-autologous "public" targets antibody-target pairs immune response Leads **Fv** Regior **Hit Antibodies** Weaponization Fc Region Activating Fc Fc + binding domain Fc + small molecule (e.g., T cell engager) (e.g., ADC)

ADC, antibody-drug conjugate; Fc, fragment crystallizable; Fv, variable fragment.

### ATRC-101 Represents the Potential of the Atreca Approach



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



Lung adenocarcinoma patient undergoing treatment with nivolumab

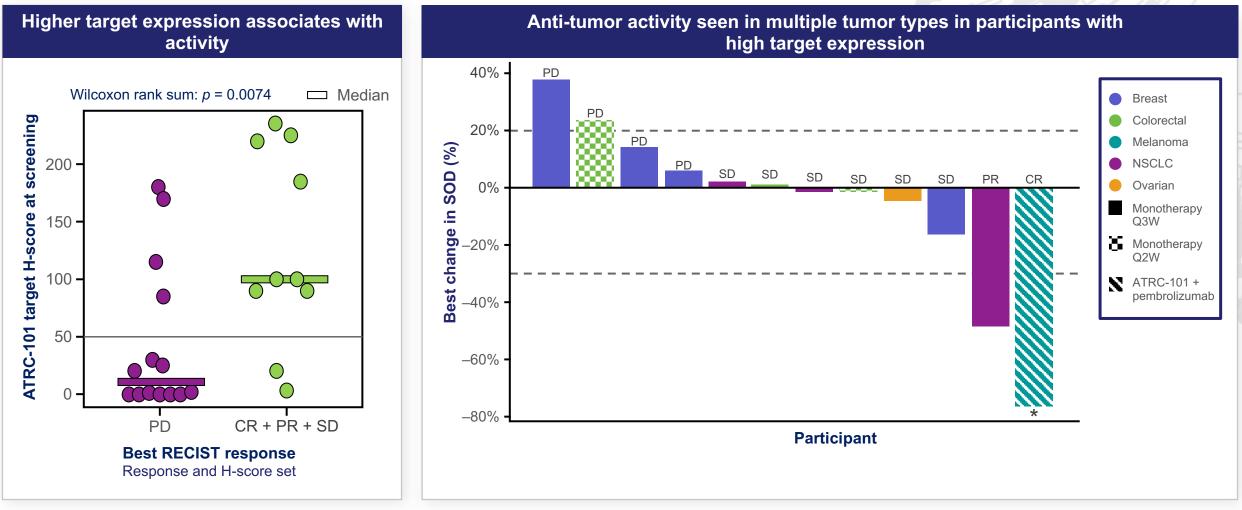


ATRC-101 binds an RNP complex present on multiple tumor types across patients

- First-in-class program
  - Novel target
  - Novel MOA
- Phase 1b trial in select solid tumors is ongoing, enrolling participants in Q2W and Q3W monotherapy cohorts and in combination cohort with pembrolizumab
- Well-tolerated in monotherapy and combination cohorts at all dose levels evaluated

# Clinical Activity of ATRC-101 Validates Atreca's Discovery Approach and Platform





\*Lymph nodes deemed non-pathologic (<10 mm) and considered a CR.

CR, complete response; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; SOD, sum of diameters.



### Atreca's Platform Has Generated a Robust Pipeline

Candidate / Lead	Target	Format / MOA	Lead	Candidate / Preclinical	Phase 1	Phase 2	Weaponization Tech
NCOLOGY							
ATRC-101	Novel RNP Complex	IgG Antibody w/ Driver Antigen Engagement		• • • • • • • • • • • • • • • • • • •			
ATRC-301	EphA2	ADC (Cytotoxic)					<b>zyme</b> works
APN-122597	(novel epitope)	T Cell Engagement (via CD3)		•         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •           •         •	6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		
APN-497444	Glycan (tumor-specific)	ADC (Cytotoxic)			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		<b>zyme</b> works
APN-959038	Transmembrane protein (novel epitope)	ADC (Cytotoxic)					<b>zyme</b> works
APN-346958	RNA-binding protein	T Cell Engagement (via CD3)		0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0           0         0			Xencor
APN-541885	Oncofetal protein	NK & T Cell Engagement (via IL-15SA)		•         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •           •         •         •			
FECTIOUS DISEASES							
ATRC-501 / MAM01 (Malaria)	<i>P. falciparum</i> Circumsporozoite Protein	IgG antibody					
APN-850271 / APN-906072 (COVID-19)	SARS-CoV-2 Spike Protein	IgG antibody					

ADC, antibody–drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2; IgG, immunoglobulin G; IL, interleukin; MOA, mechanism of action; NK, natural killer; RNA, ribonucleic acid; RNP, ribonucleoprotein; SA, superagonist; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### The Atreca Discovery Platform

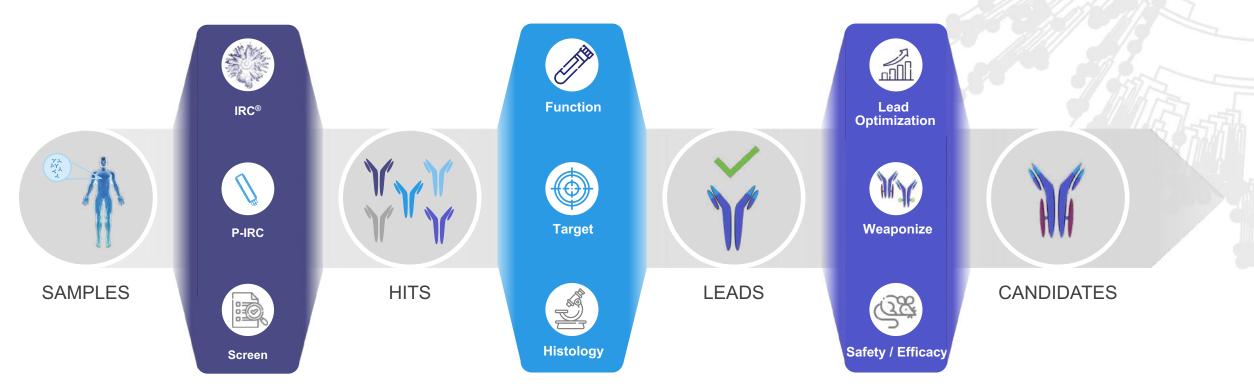
**Daniel Emerling, PhD** 

SVP, Research



### Atreca's Drug Discovery Platform

From patient anti-tumor immune responses to clinical candidates



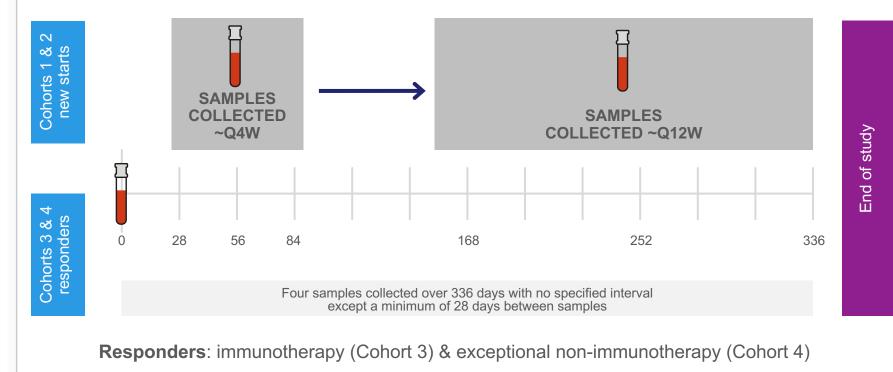
## Platform delivers candidates with potent anti-tumor activity binding novel targets and epitopes



### Sample Acquisition and Repository

Sample acquisition study design

**New starts**: immunotherapy (Cohort 1) & tumor-targeting antibody (Cohort 2)

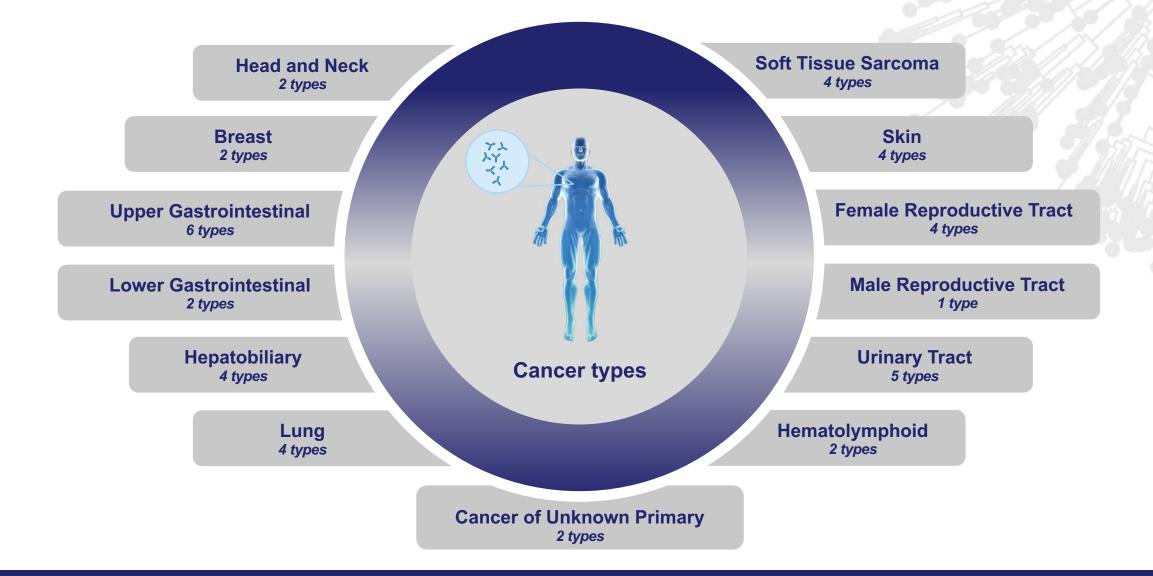


### Atreca sample repository

- Samples: >1700
- Patient donors: >500
- Solid tumor types: >35



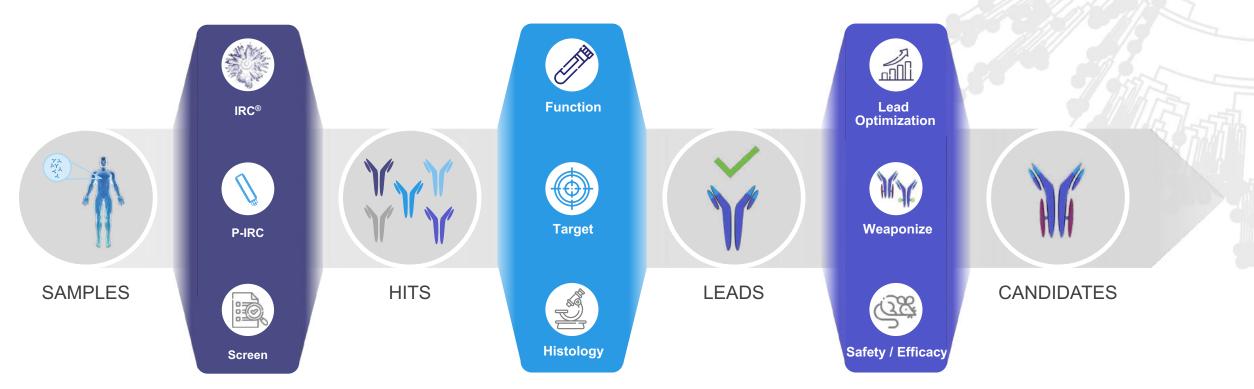
### Cancer Types Represented in the Atreca Sample Repository





### Atreca's Drug Discovery Platform

From patient anti-tumor immune responses to clinical candidates

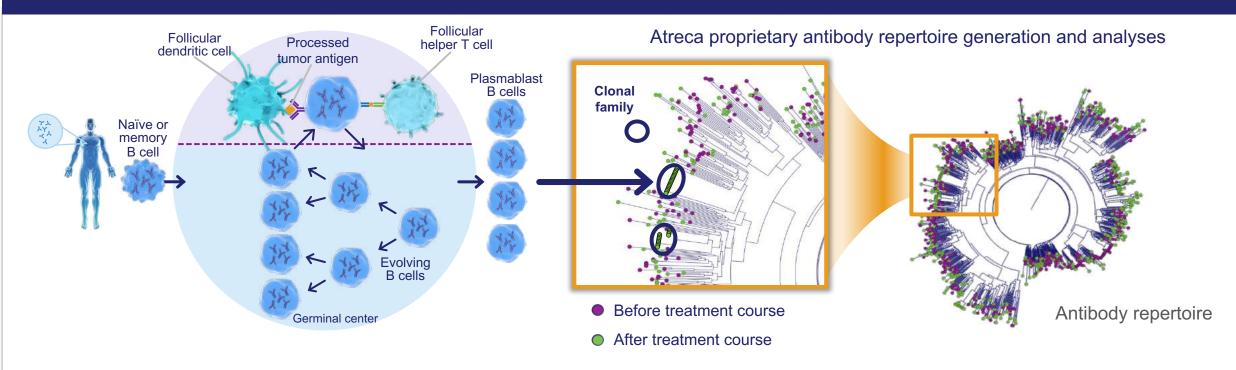


### Platform delivers candidates with potent anti-tumor activity binding novel targets and epitopes



### Atreca's Platform Leverages B Cell Biology for Discovery

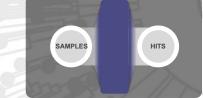
Cancer patients have an antigen-driven B cell response similar to those driven by antigens in infectious disease or autoimmunity<sup>1</sup>

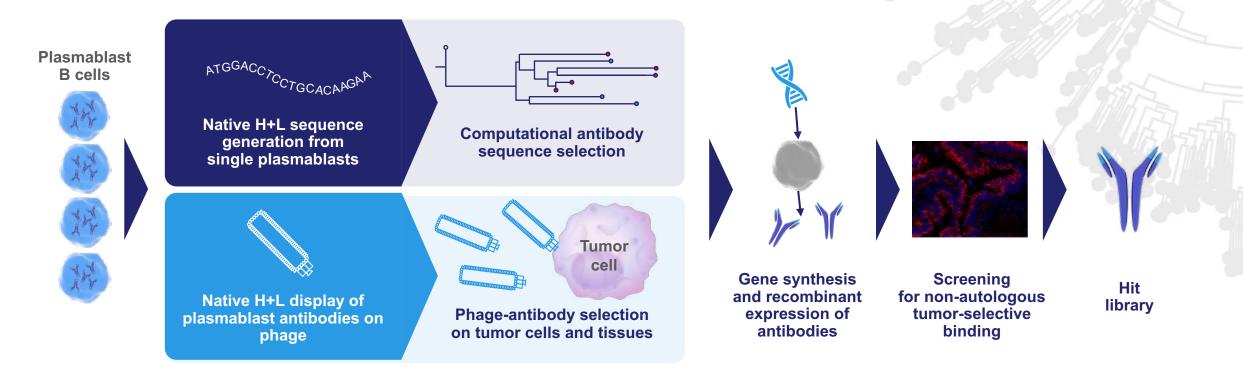


- Plasmablasts express antibodies targeting antigens being processed by the active immune response
- Clonal families of plasmablast antibodies are generated in germinal centers during an adaptive immune response

<sup>1.</sup> DeFalco J, et al. Clin Immunol. 2018;187:37-45.

Atreca Identifies Tumor-Selective "Hit Antibodies" from the Plasmablast Repertoires of Cancer Patients



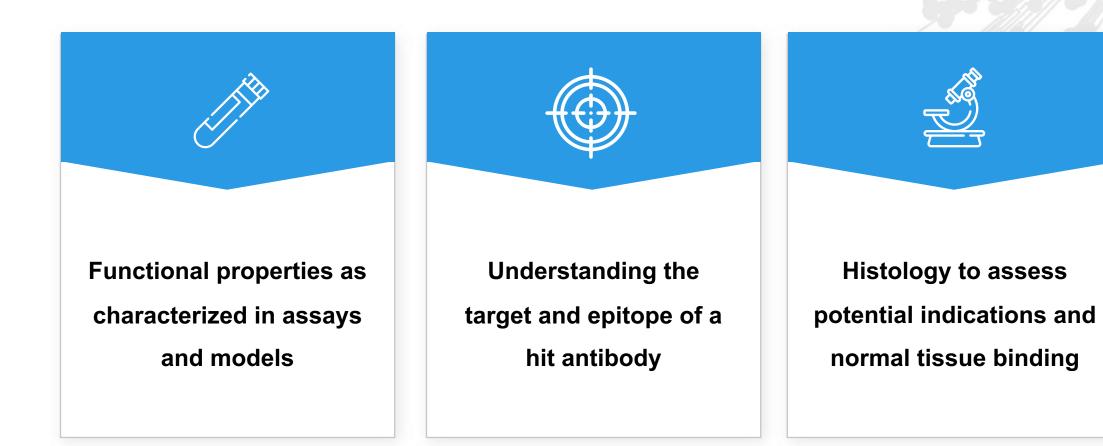


Foundational patents granted in multiple jurisdictions feature **composition of matter** claims directed to polynucleotide libraries of native pairs of antibody heavy and light chain sequences generated from plasmablasts using nucleotide barcoding at the single-cell level

Our phage-based approach is also supported by a growing patent portfolio

### Atreca's Hit-to-Lead Path

#### Leads are selected based on:



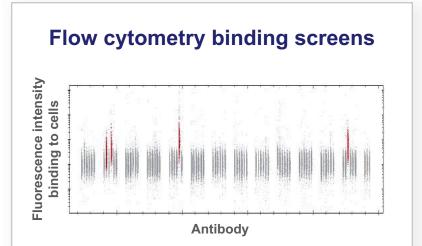
LEADS

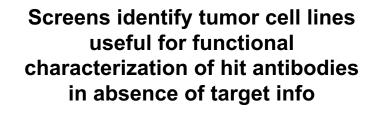
HITS

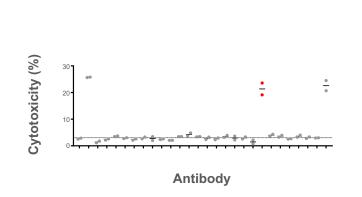
Tumor Cell Lines that Bind Hit Antibodies Enable in Vitro and in Vivo Functional Assessments



### Functional assessments performed in parallel help define early leads



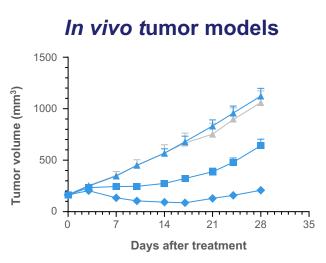




Functional in vitro screens

#### Tumor cell killing assessed using

- Effector cells to assay for potential in bispecific immune-engager formats
- Toxin conjugates to assess potential as ADC

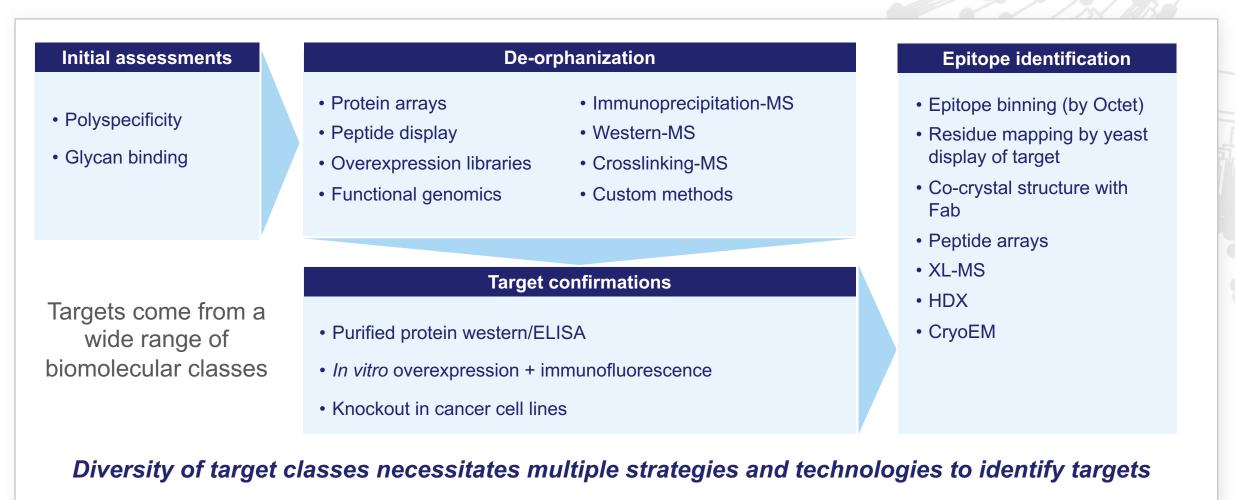


### Activity *in vivo* assessed using CDX models

- Comparison of various feasible weaponizations of early leads
- Syngeneic and xenograft models

ADC, antibody-drug conjugate; CDX, cell line-derived xenograft.

### Multiple Technologies Enable Identification of the Novel Targets and Epitopes of Tumor-Binding Hit Antibodies



ELISA, enzyme-linked immunosorbent assay; EM, electron microscopy; Fab, fragment antigen-binding; HDX, hydrogen/deuterium exchange; MS, mass spectrometry; XL, cross-linking.

HITS

LEADS

Industrial Scale Histological Screening Possible Because Hit Antibodies Are Active as Histological Reagents



#### **APN-854213**

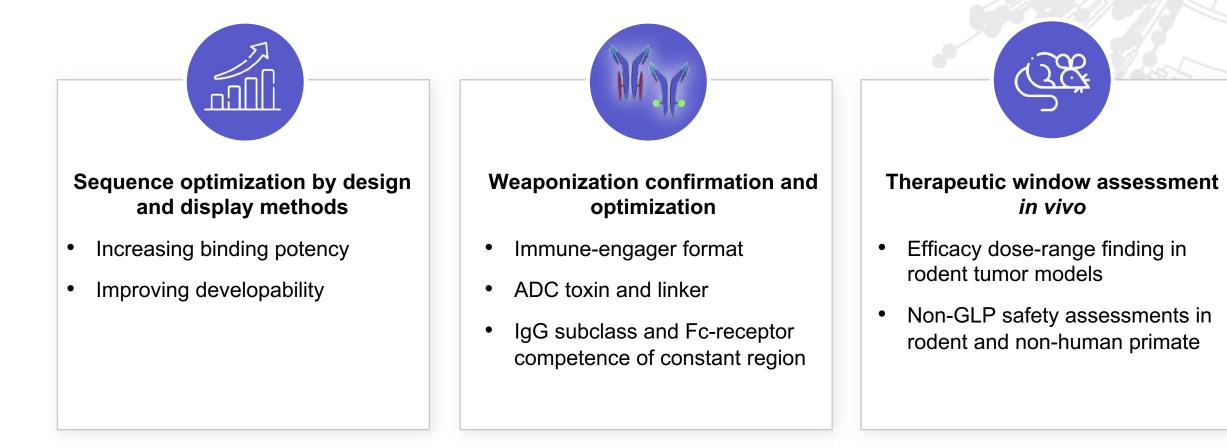
ADENOCARCINOMA Lung		NORMAL Adjacent lung
MUCINOUS ADENOCARCINOMA Ovary		NORMAL Adjacent ovary
ADENOCARCINOMA Colon		NORMAL Adjacent colon
MELANOMA Cutaneous		BENIGN Nevus

#### Staining against panels of human tumor and normal tissues reveals

- Relevant indications and prevalence
- Normal tissue binding
- Cellular and subcellular localization of epitopes
   relevant to weaponization strategy

### Atreca's Lead-to-Candidate Path

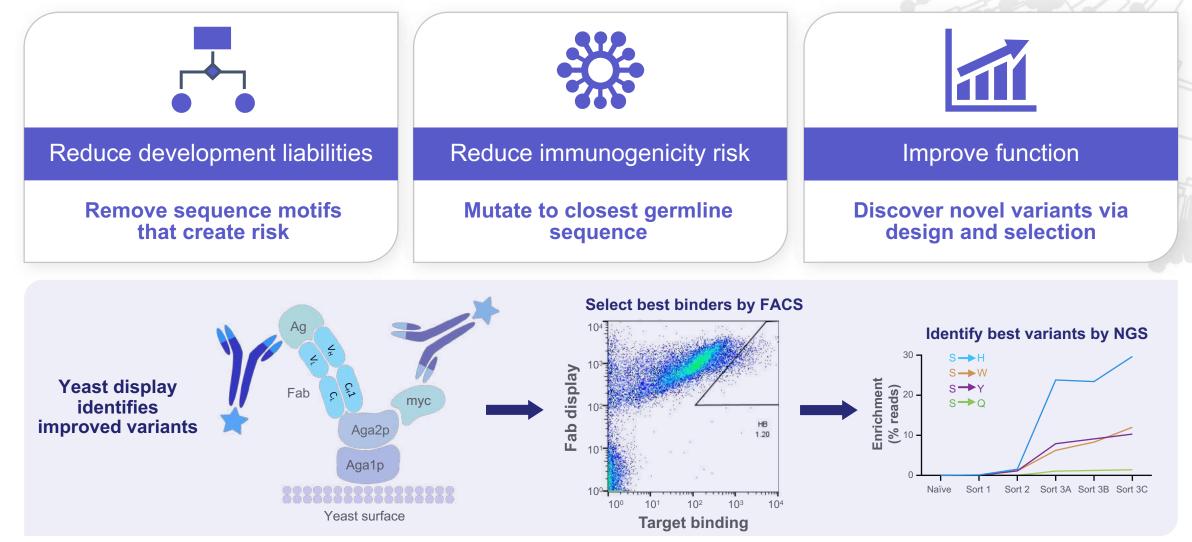
### **Optimizing human-derived antibodies for therapeutic development**



CANDIDATES

LEADS

Antibody Lead Optimization by Design and Display Methods Improves Patient Derived Antibodies



C, constant; Fab, fragment antigen-binding; FACS, fluorescence-activated cell sorting; NGS, next-generation sequencing; V, variable.

CANDIDATES

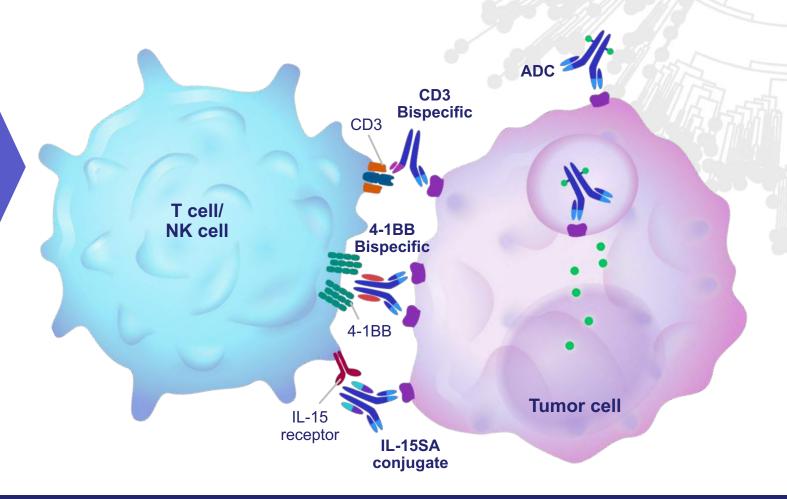
LEADS



### Antibody Weaponization Delivers Potent Tumor Killing

#### Weaponization

- Antibody-drug conjugates (ADC)
- T cell engagers (CD3)
- T & NK cell engagers (4-1BB)
- IL-15 superagonist fusion





### Atreca's Pipeline

Candidate / Lead	Target	Format / MOA	Lead	Candidate / Preclinical	Phase 1	Phase 2	Weaponization Tech
NCOLOGY							
ATRC-101	Novel RNP Complex	IgG Antibody w/ Driver Antigen Engagement		0 0 0 0 0 0			
ATRC-301	EphA2	ADC (Cytotoxic)					<b>zyme</b> works
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APN-346958	RNA-binding protein	T Cell Engagement (via CD3)		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			Xencor
APN-541885	Oncofetal protein	NK & T Cell Engagement (via IL-15SA)		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
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ATRC-501 / MAM01 (Malaria)	<i>P. falciparum</i> Circumsporozoite Protein	IgG antibody					
APN-850271 / APN-906072 (COVID-19)	SARS-CoV-2 Spike Protein	IgG antibody					

ADC, antibody-drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2; IgG, immunoglobulin G; IL, interleukin; MOA, mechanism of action; NK, natural killer; RNA, ribonucleic acid; RNP, ribonucleoprotein; SA, superagonist; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### Atreca's Anti-EphA2 Program: ATRC-301 (Clinical Candidate) APN-122597 (Lead)

Amy Manning-Bog, PhD

VP, Translational Sciences

### Alexander Scholz, PhD

Senior Director, In Vitro Pharmacology

#### Shaun Lippow, PhD

VP, Protein Engineering

### **Executive Summary**

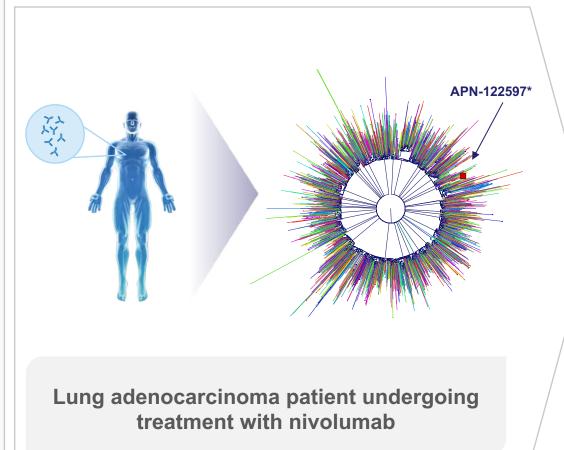


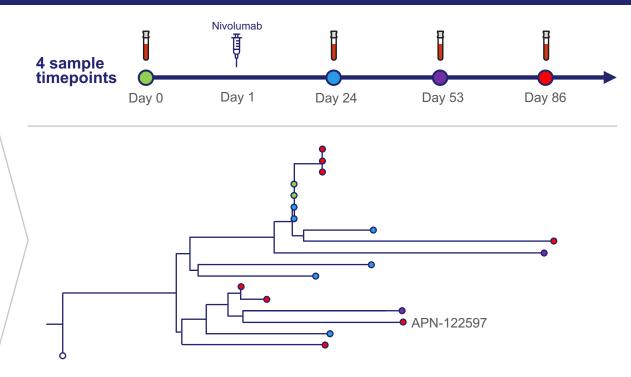
- Our antibodies recognize a novel, membrane-proximal epitope on EphA2
- >50% epitope prevalence in patient samples from 12 different cancer indications
- No impactful staining observed on normal human tissue in non-GLP studies
- Optimization significantly improved lead antibody potency and developability
- Potent activity in ADC, CD3-engager, and 4-1BB agonist bispecific formats
- Significant reduction in tumor volume using multiple formats *in vivo* with no significant toxicity signals yet observed
- Minimal to no effect on downstream EphA2 signaling
- Atreca's anti-EphA2 program clearly differentiated from other former or current clinical programs targeting EphA2

### EphA2 Reactive B Cell Lineage Identified in Plasmablasts of a Lung Cancer Patient



#### Lead antibody APN-122597 discovered via the Atreca platform





#### Eighteen plasmablasts from 4 timepoints with 13 unique antibody clones

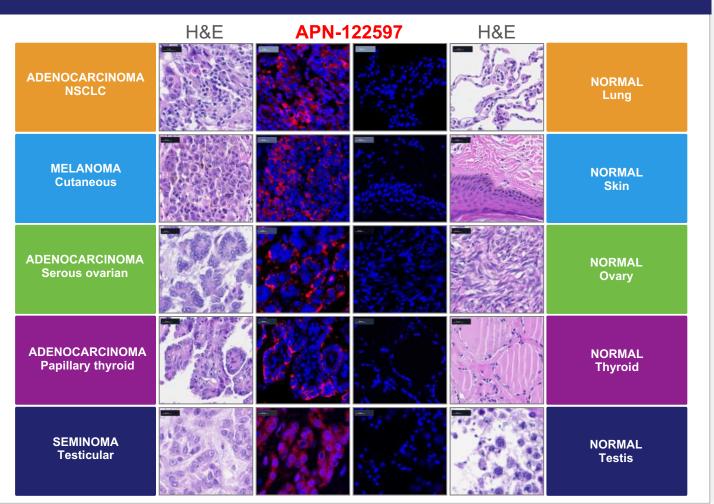
- Lineage is present from the first timepoint and expands following nivolumab
- APN-122597 is observed in fourth sample

# Anti-EphA2 Antibody Binds to Human Tumor but not to Normal Tissue & Recognizes its Target on the Cell Surface

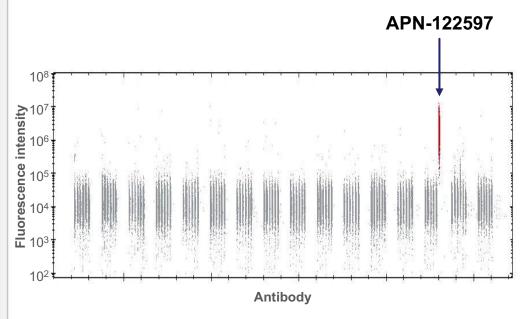


**APN-122597** reactivity is tumor-specific across multiple cancer types

APN-122597 was identified as a strong binder to human tumor cell lines by high-throughput flow cytometry



EphA2, erythropoietin-producing hepatocellular receptor A2; H&E, hematoxylin and eosin; NSCLC, non-small cell lung cancer.



- Time-resolved histogram: high-throughput screening assay to detect cell surface binding
- Each column shows fluorescence intensity of human prostate cancer cells stained with a different antibody from a 96-well plate

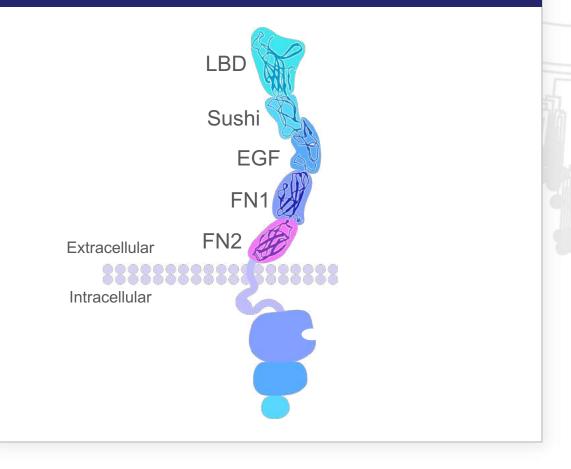


### EphA2: A Validated and Potentially High Value Target

- Eph proteins are the largest family of receptor tyrosine kinases (RTKs) known in humans
- RTKs are a proven target class in treatment of solid tumors
- Eph receptors regulate cell-to-cell communication, plasticity, and patterning
- Ephrins are the cell surface-bound ligands of Eph receptors
- EphA2 is one of 14 Eph receptors that predominantly bind ephrin A ligands
- Only low levels of EphA2 are normally expressed in the adult in non-tumor tissues
- EphA2 is overexpressed in many cancers including:

Prostate	Esophageal	Ovarian
Melanoma	Gastric	Bladder
Colon	Breast	Lung
Glioma	Cervical	

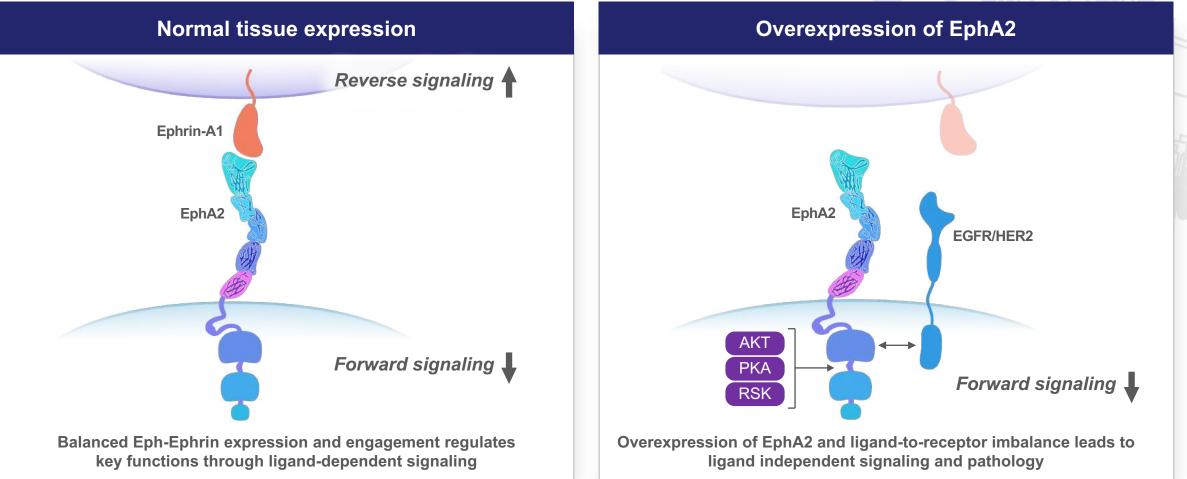
#### EphA2 receptor domain structure



EGF, epidermal growth factor-like; Eph, erythropoietin-producing hepatocellular; EphA2, erythropoietin-producing hepatocellular receptor A2; FN, fibronectin; LBD, ligand-binding domain.



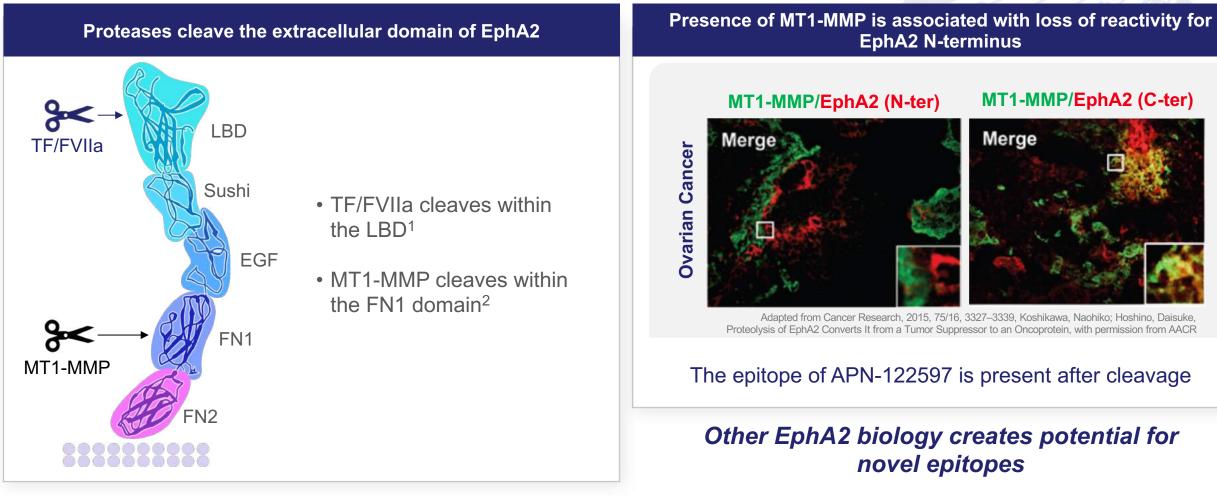
### Balanced Ligand-Driven Signaling Mediates Eph Function Unbalanced receptor signaling drives pathology



EGFR, epidermal growth factor receptor; Eph, erythropoietin-producing hepatocellular; EphA2, erythropoietin-producing hepatocellular receptor A2; HER2, human epidermal growth factor receptor 2; PKA, protein kinase A; RSK, ribosomal s6 kinase.

## EphA2 Tumor Biology Can Potentially Prevent Binding by Agents That Target the Ligand Binding Domain

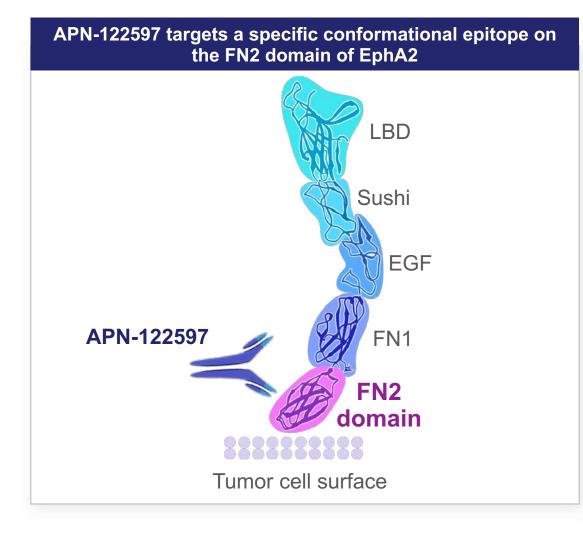




EGF, epidermal growth factor-like; EphA2, erythropoietin-producing hepatocellular receptor A2; F, factor; FN, fibronectin; LBD, ligand-binding domain; MTI-MMP, membrane type 1 matrix metalloproteinase; TF, tissue factor. 1. Eriksson O, et al. *J Biol Chem.* 2014;289:32379–32391; 2. Koshikawa N, et al. *Cancer Res.* 2015;75:3327–3339.



### Atreca's Anti-EphA2 Antibodies Target a Novel Epitope



#### Epitope of APN-122597 confirmed by co-crystal structure

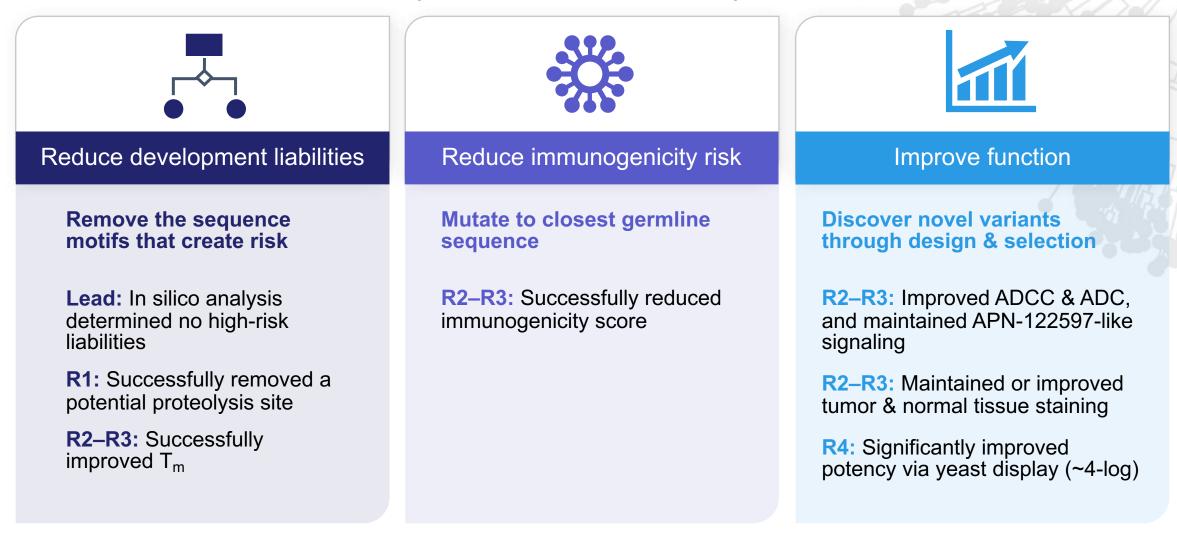
- Yeast display utilized to delineate epitope
- Epitope is conformational and spans four stretches of sequence in FN2 domain
- Epitope residues are not conserved in other Eph family members
- Epitope residues are conserved across tox species

### Epitope distinct from those targeted by biologics previously or currently in clinical development

EGF, epidermal growth factor-like; Eph, erythropoietin-producing hepatocellular; EphA2, erythropoietin-producing hepatocellular receptor A2; FN, fibronectin; LBD, ligand-binding domain.

Antibody Lead Optimization Yielded Significant Improvements in Potency and Developability

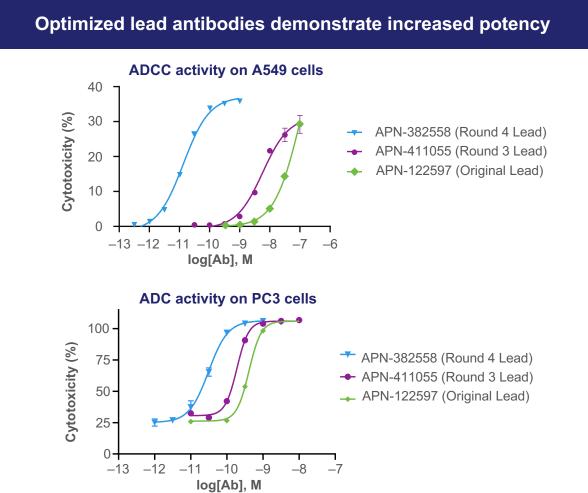






### **Optimized Leads Are Developable and Potent**

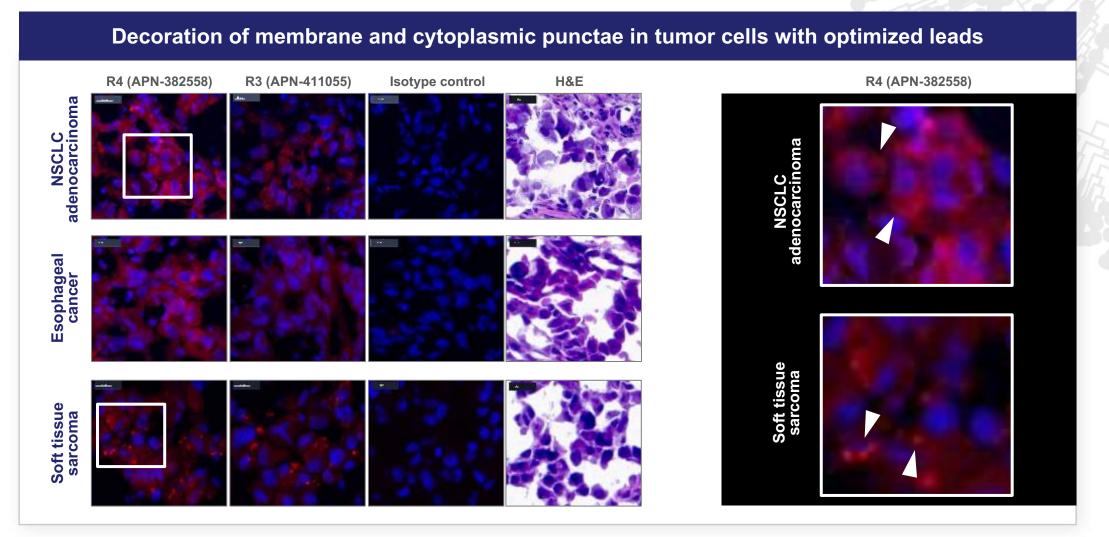
	APN-122597	APN-411055	APN-382558
Antibody	Lead	Optimized R3	Optimized R4
Mutations from lead, n	0	5	9
Predicted high-risk liabilities, n	0	0	0
Predicted medium-risk liabilities, n	1	0	0
Predicted immunogenicity risk	Low	Low	Low
BVP binding	0	0	0
<b>T</b> <sub>m</sub> (° <b>C</b> )	64.8	64.7	66.4
Monovalent binding affinity	2000 nM	1000 nM	20 nM
A549 cell binding EC <sub>50</sub>	400 nM	30 nM	1 nM
A549 ADCC EC <sub>50</sub>	30 nM	3 nM	0.006 nM



ADC, antibody-drug conjugate; ADCC, antibody-dependent cellular cytotoxicity; BVP, baculovirus particles; EC<sub>50</sub>, half maximal effective concentration; R, round; T<sub>m</sub>, melting temperature.



### **Optimized Leads Possess Enhanced Tumor Binding**

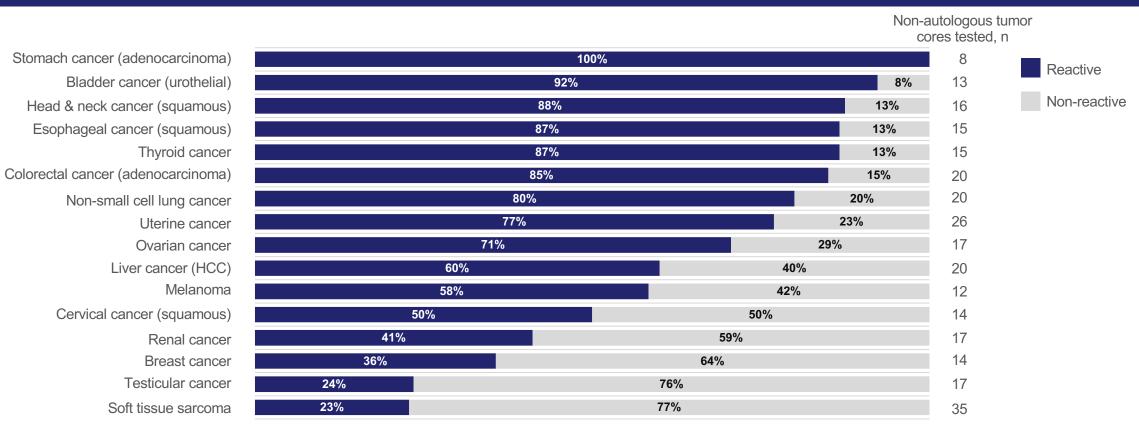


H&E, hematoxylin and eosin; NSCLC, non-small cell lung cancer; R, round.



### Atreca's Anti-EphA2 Antibodies Bind Multiple Tumor Types

#### Tumors considered reactive if APN-382558 demonstrated detectable signal in >30% malignant cells per core

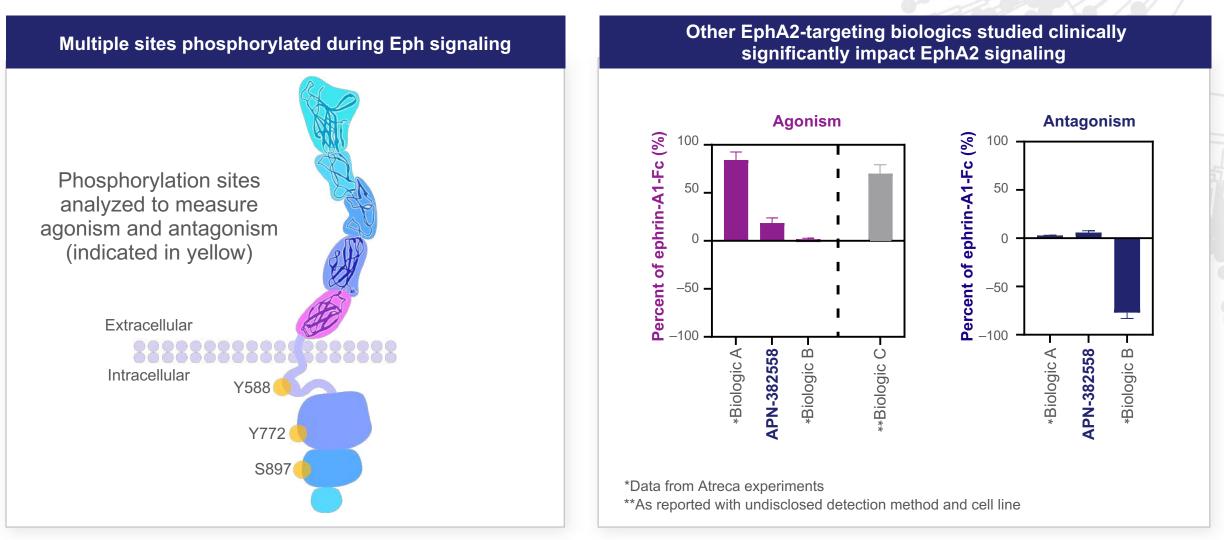


#### No appreciable signal (including membrane decoration) was detected in 26 normal human tissues by IHC

EphA2, erythropoietin-producing hepatocellular receptor A2; HCC, hepatocellular carcinoma; IHC, immunohistochemistry.

# Atreca's Anti-EphA2 Antibodies Minimally Impact the EphA2-EphrinA1 Signaling Axis





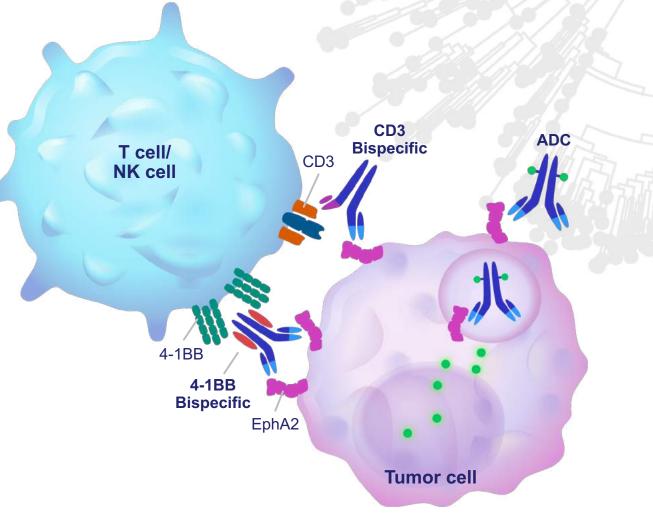
Eph, erythropoietin-producing hepatocellular; EphA2, erythropoietin-producing hepatocellular receptor A2; Fc, fragment crystallizable.



## Antibody Weaponization Delivers Potent Tumor Killing

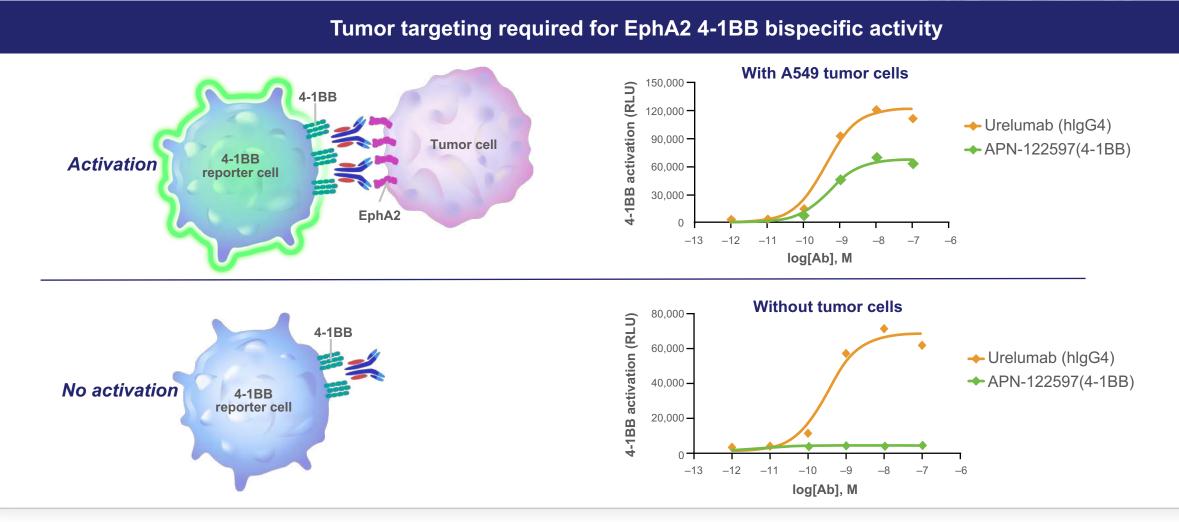
#### **EphA2 Weaponization**

- T & NK cell activators (4-1BB)
- T cell engagers (CD3)
- Antibody-drug conjugates (ADC)



# EphA2-targeting 4-1BB Bispecific Active *in Vitro* Only in Presence of Human Tumor Cells



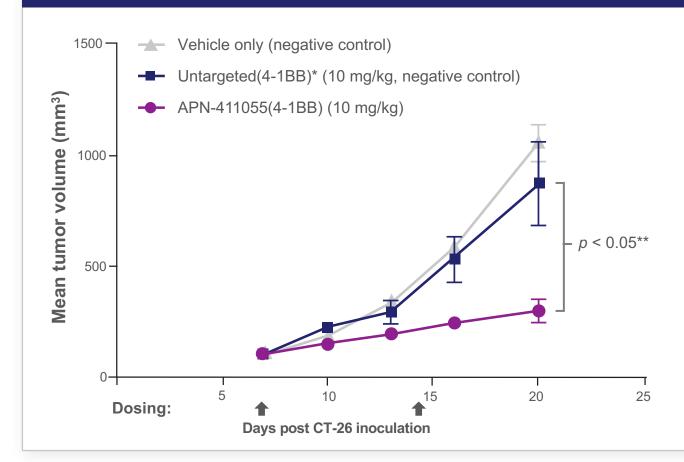


EphA2, erythropoietin-producing hepatocellular receptor A2; hlgG4, human immunoglobulin G4; RLU, relative light unit.

### 4-1BB Bispecific Version of Atreca Anti-EphA2 Antibody Reduces Tumor Growth Significantly *in Vivo*



R3 optimized lead APN-411055 drives tumor reduction in a 4-1BB agonist bispecific format

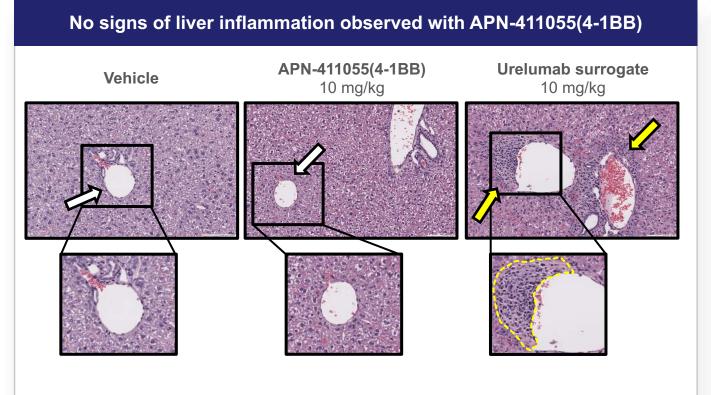


- Standard syngeneic CT-26 model
- Treatment of established tumors
- Robust effects on tumor growth compared to untargeted 4-1BB
- Survival as compared to untargeted 4-1BB also significantly longer (log rank, *p* < 0.001)</li>
- No body weight or other changes noted

\*Anti-hen egg lysozyme "targeting" 4-1BB bispecific, control for EphA2 targeting of 4-1BB. \*\*One-sided Wilcoxon rank sum test for normalized area above the curve at end of study. EphA2, erythropoietin-producing hepatocellular receptor A2; R, round.



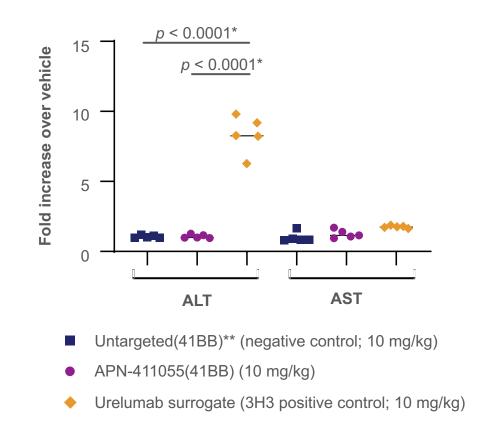
## 4-1BB Bispecific Does Not Cause Signs of Liver Damage



- Atreca 4-1BB bispecific shows no breach of portal vein
- Urelumab surrogate causes lymphocytic infiltration into liver parenchyma

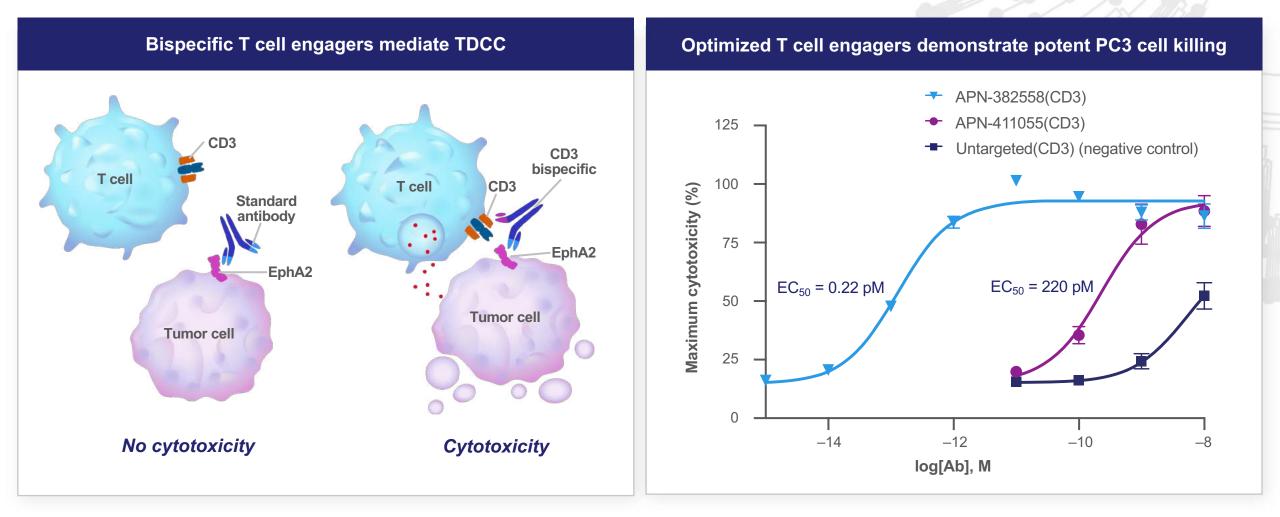
\*One-way ANOVA. \*\*Anti-hen egg lysozyme "targeting" 4-1BB bispecific, control for EphA2 targeting of 4-1BB. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

APN-411055(4-1BB) does not increase ALT *in vivo* like the urelumab surrogate



## Anti-EphA2 Antibody as CD3 T Cell Engager Demonstrates Sub-Picomolar *in Vitro* Cell Killing



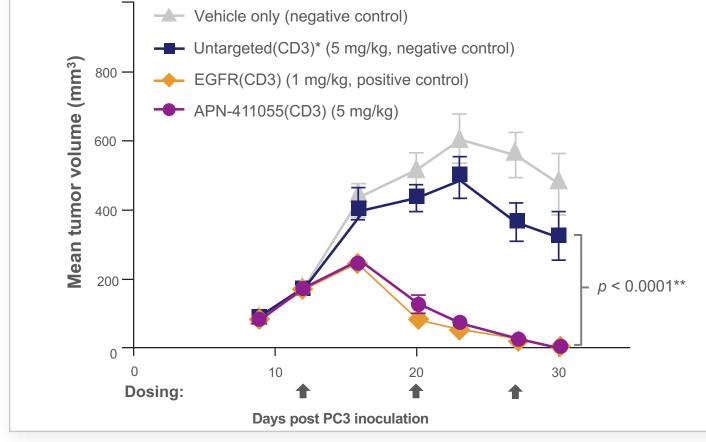


Ab, antibody; EC<sub>50</sub>, half maximal effective concentration; EphA2, erythropoietin-producing hepatocellular receptor A2; TDCC, T cell-dependent cellular cytotoxicity.

CD3 T Cell Engager Version of Atreca Anti-EphA2 Antibody Drives Significant Tumor Regression *in Vivo* 



#### In vivo tumor reduction with the R3 optimized lead APN-411055 in a CD3 bispecific format



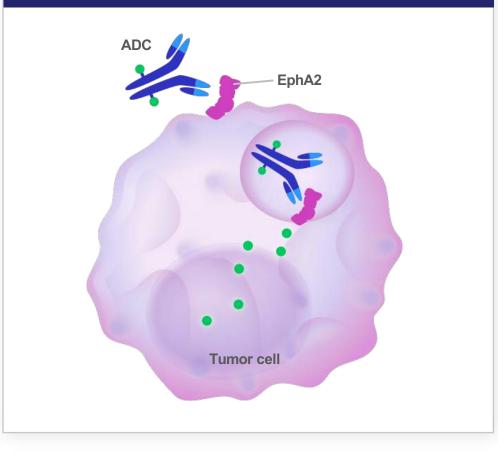
- Standard humanized mouse model
- Treatment of established tumors
- Weekly IP dosing
- Significant tumor regression/elimination
- No significant body weight changes
- Advancing an EphA2 in CD3 engager format

\*Anti-hen egg lysozyme "targeting" 4-1BB bispecific, control for EphA2 targeting of 4-1BB. \*\*One-sided Wilcoxon rank sum test for normalized area above the curve at Day 30. EGFR, epidermal growth factor receptor; EphA2, erythropoietin-producing hepatocellular receptor A2; IP, intraperitoneal; R, round.



## Zymeworks Technology Driving Atreca ADCs

#### ADCs mediate tumor cell killing directly



ZymeLink<sup>™</sup> technology highlights

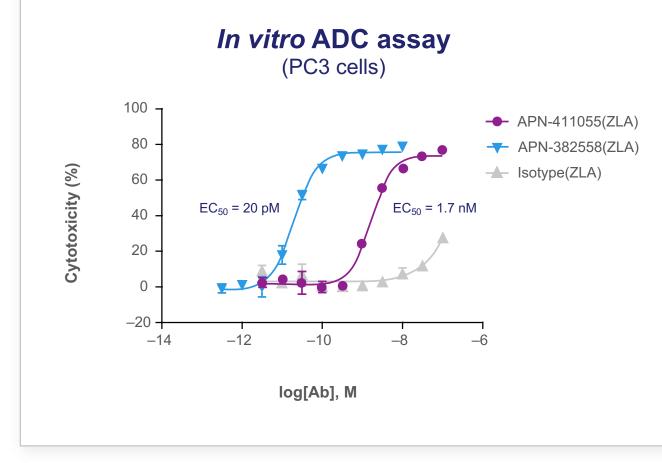
- Uses proprietary auristatin-based linker-payload that inhibits cell division by blocking tubulin polymerization
- Closely resembles natural antibodies with potential for improved pharmacokinetics, stability, and cytotoxin exposure
- Designed for increased tolerability
- Supports a wide therapeutic window

ADC, antibody–drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2.



### Atreca's Anti-EphA2 ADCs Show Potent in Vitro Activity

Successful conjugation with Zymeworks' auristatin linker-payload technology (ZLA)



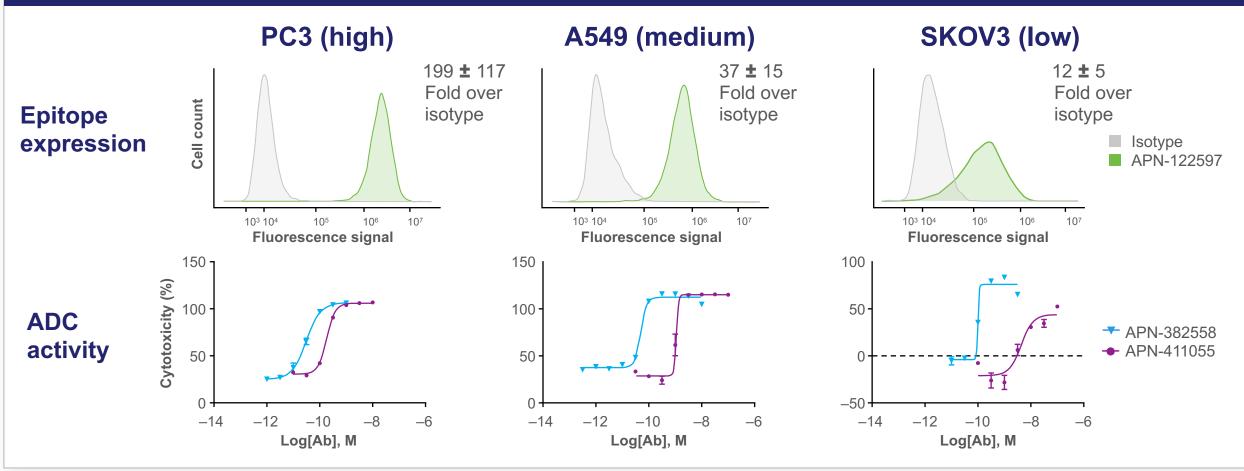
- Conjugation of Atreca's EphA2-targeting antibodies with ZLA technology at DAR 3
- Final ADC shows potent and specific cytotoxic activity on EphA2 expressing cells *in vitro*
- Strong improvements in potency observed going from Lead Optimization round 3 to 4

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; EC<sub>50</sub>, half maximal effective concentration; EphA2, erythropoietin-producing hepatocellular receptor A2.

## Optimized Anti-EphA2 Leads Maintain Potent ADC Activity in Vitro Across a Range of Epitope Expression Levels



Most potent binder maintains activity despite reduced receptor density



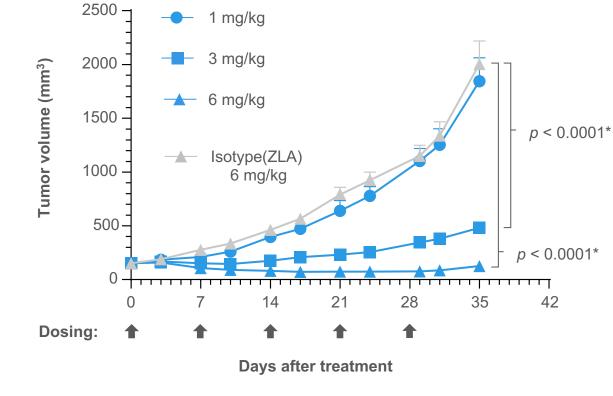
ADC assay using secondary anti-mouse Fab DMDM.

ADC, antibody-drug conjugate; DMDM, duocarmycin DM; EphA2, erythropoietin-producing hepatocellular receptor A2; Fab, fragment antigen-binding.

## Optimized Lead Antibody Shows Potent Anti-Tumor Activity in ZymeLink Auristatin (ZLA) Format



APN382558(ZLA) demonstrates anti-tumor activity in vivo



#### APN-382558(ZLA) in PC3 model

- APN-382558(ZLA) induces dose-dependent anti-tumor activity in the PC3 CDX model
- No significant reduction in body weight observed compared to vehicle control group
  - Single doses of up to and including **30 mg/kg** in rats were well-tolerated with no significant safety signals around coagulation and on other tox parameters

\*One-sided Wilcoxon rank sum test for normalized area above the curve at Day 35.

CDX, cell line-derived xenograft; EphA2, erythropoietin-producing hepatocellular receptor A2.

## Atreca's Anti-EphA2 Program Differentiated from Previous and Current Clinical-Stage Programs



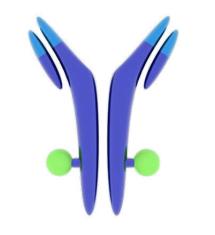
#### Points of differentiation for Atreca's anti-EphA2 program

- Novel membrane-proximal epitope
- High epitope prevalence across and within indications
- Minimal agonist and no antagonist activity
- Differentiated tumor tissue reactivity

- Minimal normal tissue reactivity
- Portfolio of potently binding optimized antibodies
- Activity demonstrated in a variety of weaponized formats
- Initial safety studies suggest substantial therapeutic window for ADC format



## ATRC-301: Atreca's Anti-EphA2 ADC Clinical Candidate



#### APN-382558(ZLA)

Several backups advancing as well

#### **Upcoming milestones**

- IND enabling activities for candidate and backup molecules have been initiated
- Non-GLP NHP toxicology data expected 2H 2022
- IND filing expected 2H 2023
- FIH study expected 1H 2024 in solid tumors including gastrointestinal and gynecological

ADC, antibody–drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2; FIH, first-in-human; GLP, good laboratory practices; IgG4, immunoglobulin G4; IND, investigational new drug; NHP, non-human primates; ZLA, ZymeLink Auristatin.

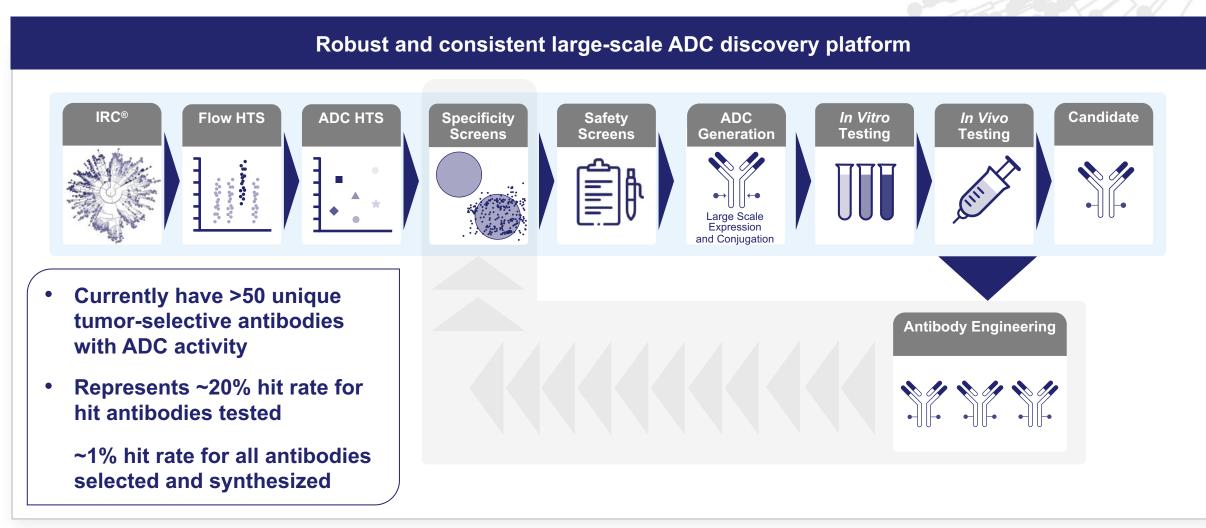
Lead Stage ADC Programs: APN-497444 (Lead) APN-959038 (Lead)

**Alexander Scholz**, PhD

Senior Director, In Vitro Pharmacology

### Atreca's ADC Engine Creates a Rich Starting Point for Clinical Candidate Generation



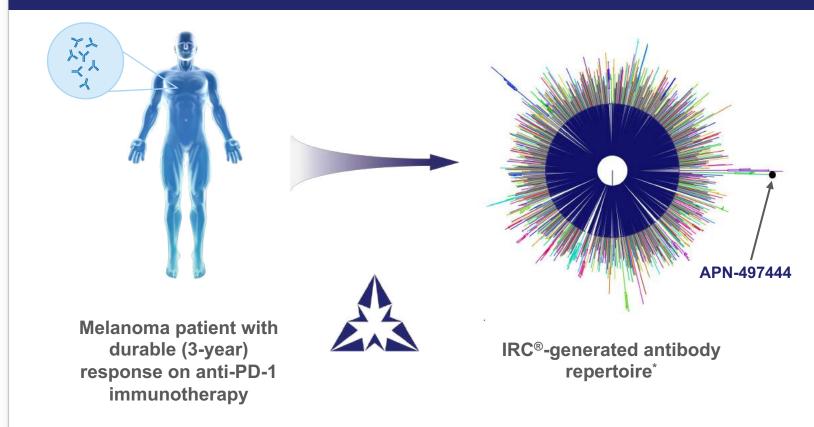


Hit antibody = selective human tumor binding. ADC, antibody-drug conjugate; HTS, high-throughput screening; IRC, Immune Repertoire Capture.



### APN-497444: A Tumor-Specific Anti-Glycan Antibody

Lead antibody APN-497444 discovered via the Atreca platform



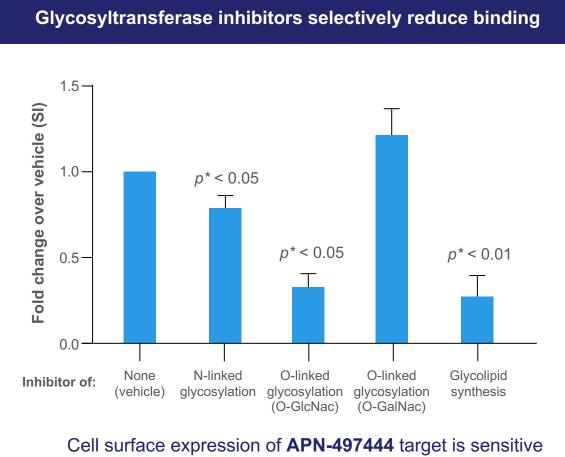
#### Lead highlights

- Strong evidence of affinity maturation in sequence
- Binds to non-autologous human tumors with high selectivity
- Selectively binds human tumor cell lines
- Recognizes a surface-expressed glycan target

\*Branches differentially colored by lineage. IRC, Immune Repertoire Capture; PD-1, programmed cell death 1.

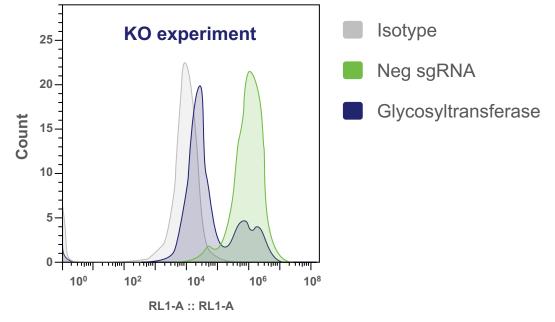


## APN-497444 Recognizes a Tumor-Specific Glycan Epitope



to selective glycosyltransferase inhibitors

\**p*-value = one-sided, paired Student's t-test against vehicle. SI, stain index; sgRNA, single guide RNA. Modulating expression of a specific glycosyltransferase affects binding of APN-497444 in flow cytometry



- Knockout of a specific glycosyltransferase inhibits cell-surface binding of APN-497444 (shown)
- Overexpression of that specific glycosyltransferase increases cell-surface binding by antibody

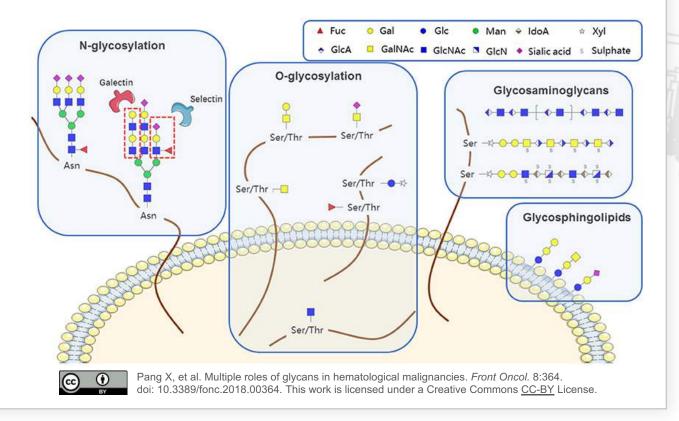
### Tumor-associated Carbohydrate Antigens (TACAs) Are Attractive Cancer Targets



#### Anti-TACA Antibodies with Therapeutic Potential Are Identified via Atreca's Discovery Platform

- Aberrant glycosylation known to be a hallmark of tumor malignancies for decades
- Multiple TACA antibodies are currently being explored in clinical trials
- Dinutuximab and naxitamab (both anti-GD2 antibodies) have received FDA approval for treatment of neuroblastoma
- Potent and selective anti-TACA antibodies are challenging to generate via standard immunization procedures

## 20% of Atreca's tumor-selective and ADC-active antibodies bind glycan targets



ADC, antibody-drug conjugate; anti-GD2, anti-disialoganglioside; FDA, US Food and Drug Administration.

### Robust and Tumor-Specific Reactivity Detected on Multiple Human Cancer Types



#### APN-497444 displays widespread yet tumor-selective binding

	Ovary	Lung	Pancreas	Esophagus			
	and a second second				Indication	Percent reactive	Total cores scored
Tumor			2 - 2 a 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 -		Ovarian cancer	71%	7
			rand		Lung cancer	60%	10
					Colorectal cancer	60%	20
Normal		Band and the second sec			Pancreatic cancer	50%	18
					Esophageal cancer	50%	10
					Prostate cancer	22%	18
				No.	Thyroid cancer	20%	20

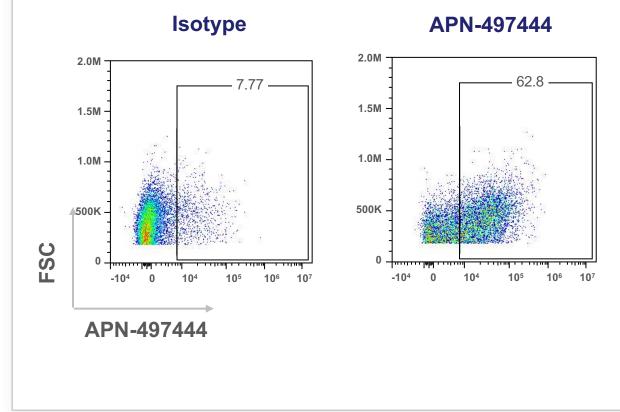
No significant reactivity or membrane signal detected in 27 normal human tissues by IHC

IHC, immunohistochemistry.

## APN-497444 Recognizes a Target on the Surface of Human Colorectal Carcinoma Cells



Flow cytometry of dissociated human tumor tissue reveals cell-surface binding

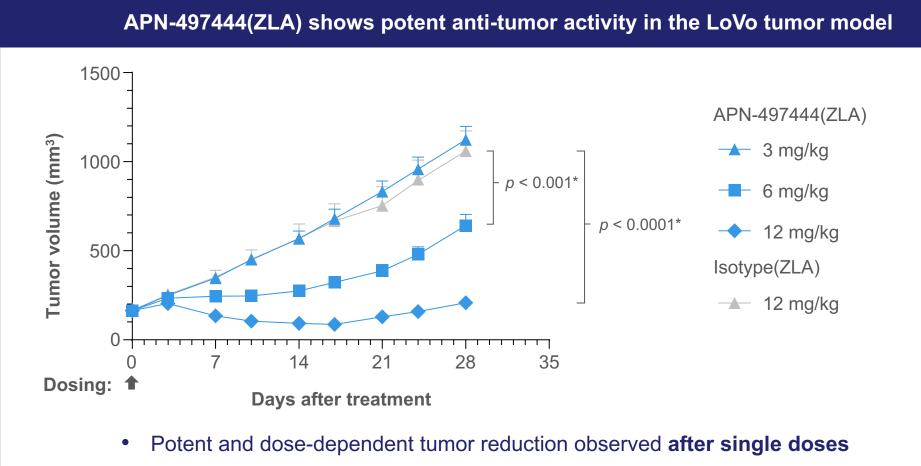


Subtype	Samples bound
Splenic flexure	0/1
Colon	2/2
Rectum	1/2
Total	3/5

- **APN-497444** bound to the surface of 3 out of 5 dissociated colorectal cancer samples
- Antibody does not recognize target on CD45<sup>+</sup> tumor-infiltrating immune cells

APN-497444 Shows Potent *in Vivo* Activity in ZymeLink-Auristatin (ZLA) Format in a Colorectal Cancer Model





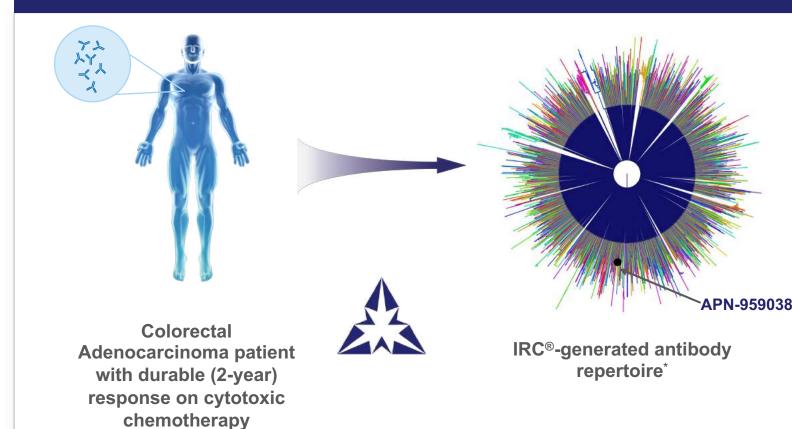
• No significant reduction in body weight observed compared to isotype control

\*One-sided Wilcoxon rank sum test for normalized area above the curve at Day 28.



## APN-959038: A New Angle on a Known Cancer Target

Lead antibody APN-959038 discovered via the Atreca platform

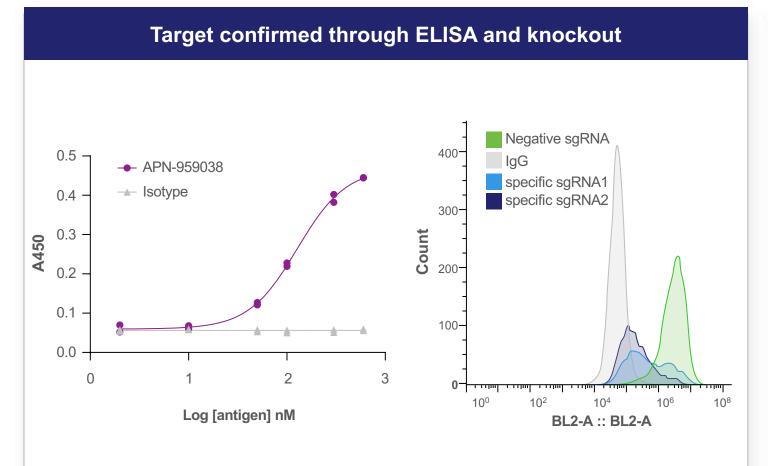


#### Lead highlights

- Identified from an expanded lineage
- Binds to non-autologous human tumor with high selectivity
- Recognizes a surface-expressed target
- Selectively binds human tumor cell lines
- No high-risk sequence-based liabilities

## APN-959038 Recognizes a Well-Described Cancer Target via a Novel Epitope





#### Current data indicate that APN-959038 binds a novel epitope

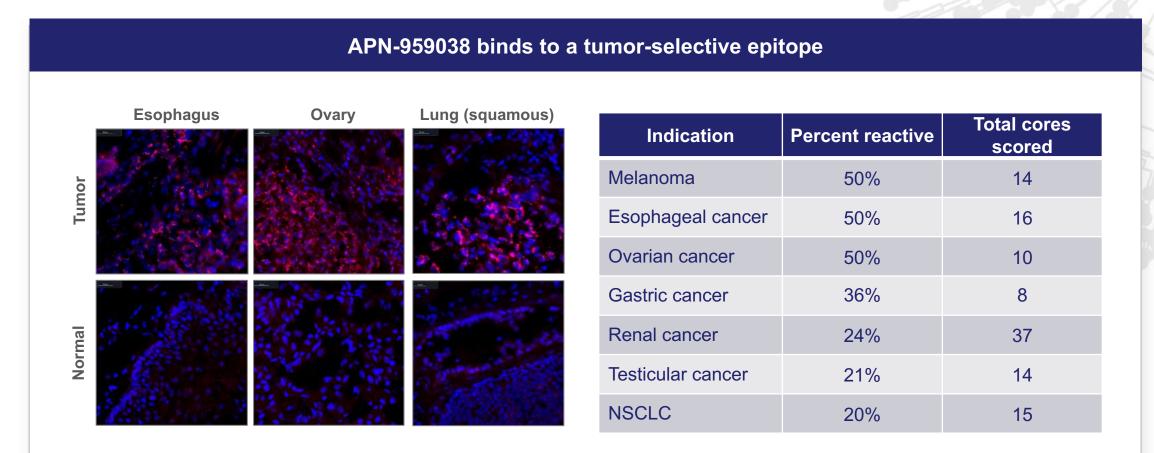
APN-959038 target features

- The target of APN-959038 is
  - Single-pass transmembrane protein
  - Overexpressed in multiple human cancer types
  - Internalizer with rapid kinetics
  - Attractive ADC target
- Prior clinical development by others as an ADC was limited due to on-target, off-tumor toxicity
- Atreca targets a novel epitope which may help overcome that limitation

ADC, antibody-drug conjugate; ELISA, enzyme-linked immunosorbent assay; IgG, immunoglobulin G; sgRNA, single guide RNA.

## APN-959038 Shows Robust and Tumor-Selective Immunoreactivity





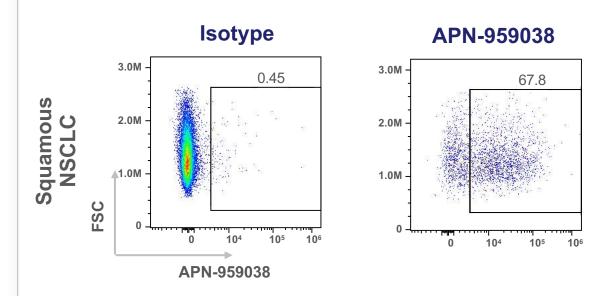
No significant reactivity detected in 27 normal human tissues by IHC

IHC, immunohistochemistry; NSCLC, non-small cell lung cancer.

APN-959038 Recognizes an Epitope on its Target Accessible on the Surface of Human NSCLC Cells



Flow cytometry of dissociated human tumor tissue reveals cell-surface binding



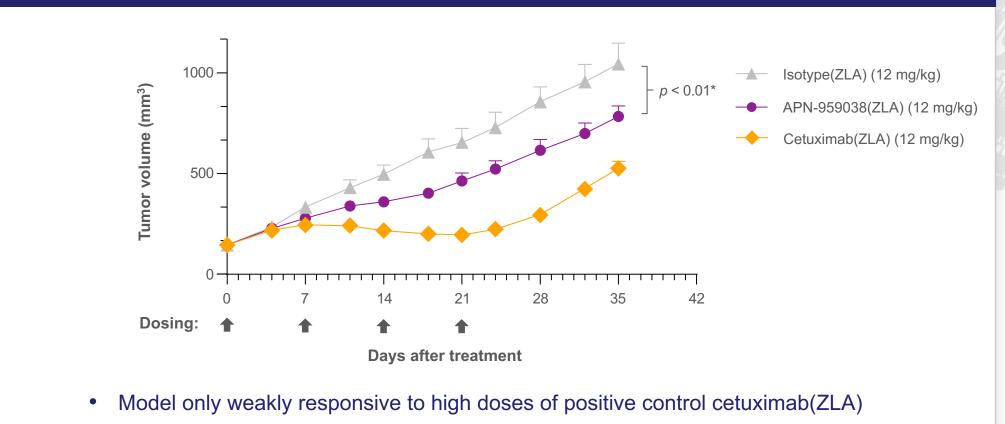
Subtype	Samples bound		
Adenocarcinoma	1/2		
Squamous cell carcinoma	4/4		
Undetermined	0/2		

- **APN-959038** bound to the surface of 5 out of 8 dissociated NSCLC cancer samples
- Surface reactivity was preferentially detected in NSCLC of the squamous subtype
- Antibody does not recognize target on CD45<sup>+</sup> tumor-infiltrating immune cells

## APN-959038(ZLA) Shows Tumor Growth Inhibition in a Fast-Growing CDX Model



APN-959038(ZLA) demonstrates significant tumor growth inhibition in the SK-BR-3 model

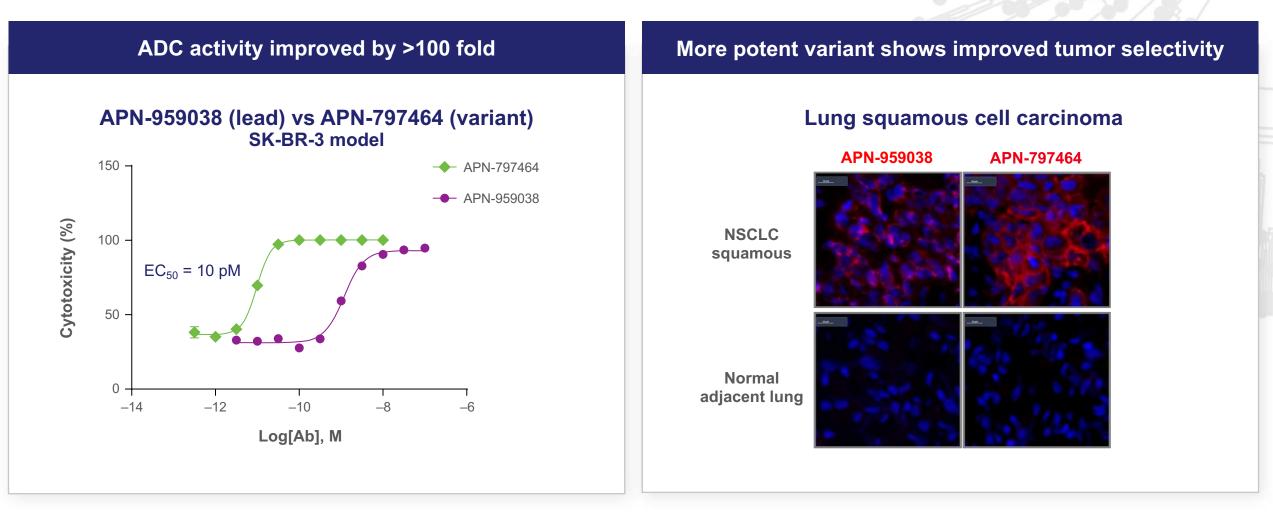


• No significant loss in body weight observed compared with isotype control group

\*One-sided Wilcoxon rank sum test for normalized area above the curve at Day 35. CDX, cell line-derived xenograft; ZLA, ZymeLink Auristatin.

First Round of Lead Optimization Has Already Produced Variants with Significantly Improved Activity





Ab, antibody; ADC, antibody–drug conjugate; EC<sub>50</sub>, half maximal effective concentration; NSCLC, non-small cell lung cancer.



## Summary: Two Lead-stage ADC Programs Advancing



- APN-497444 recognizes a tumor-specific glycan epitope
- APN-959038 recognizes a known cancer target via a potentially novel epitope



- APN-497444 and APN-959038 display strong and tumor-selective immunoreactivity
  - No significant reactivity in normal tissues detected for either antibody

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- APN-497444(ZLA) showed potent & dosedependent tumor reduction after single doses
- APN-959038(ZLA) showed significant tumor growth inhibition



- Continuing lead optimization campaign for both molecules
- Evaluating novel variants in efficacy as well as toxicology models

#### Continuing to leverage robust ADC Engine for additional programs

ADC, antibody-drug conjugate; ZLA, ZymeLink Auristatin.

## Lead Stage CD3-Engager Program: APN-346958 (Lead)

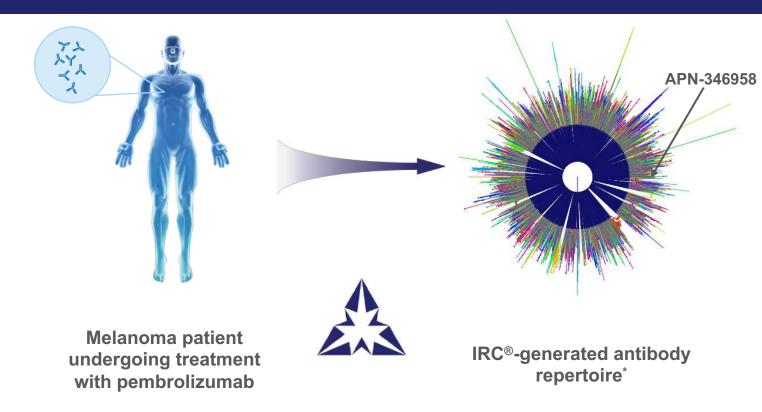
Shaun Lippow, PhD

VP, Protein Engineering

## APN-346958: A Tumor-Selective Antibody Recognizing an RNA-Binding Protein Target



#### Lead antibody APN-346958 discovered via the Atreca platform



#### Lead highlights

- Identified a lead antibody with a rare ultra-long H-CDR3
- APN-346958 selectively binds non-autologous human tumor tissue
- APN-346958 selectively binds human tumor cell lines
- No high-risk sequence-based liabilities

\*Branches differentially colored by lineage.

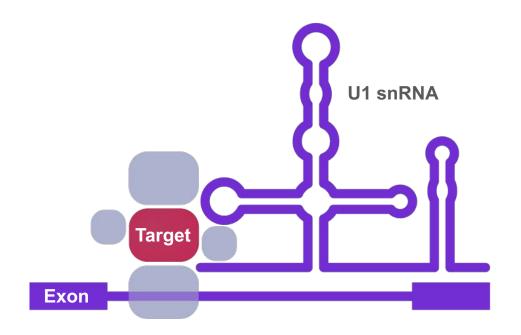
CDR, complementarity determining region; H, heavy chain; IRC, Immune Repertoire Capture; RNA, ribonucleic acid.

Novel Tumor Target: Pathological Cell-Surface Localization of a Normally Nuclear RNA-Binding Protein



#### Tumor-specific surface exposure potentially related to U1 snRNP cell-surface localization

- The target of APN-346958 is normally in the nucleus
- The target family has been shown to interact with the U1 snRNP complex
- The U1 snRNP has been detected on the surface of cells,<sup>1,2</sup> consistent with cell-surface localization of autoantibody targets<sup>3</sup> (including RNA binding proteins)
- It is hypothesized that the target of APN-346958 gets to the cell surface via a stress-driven, tumor-specific process

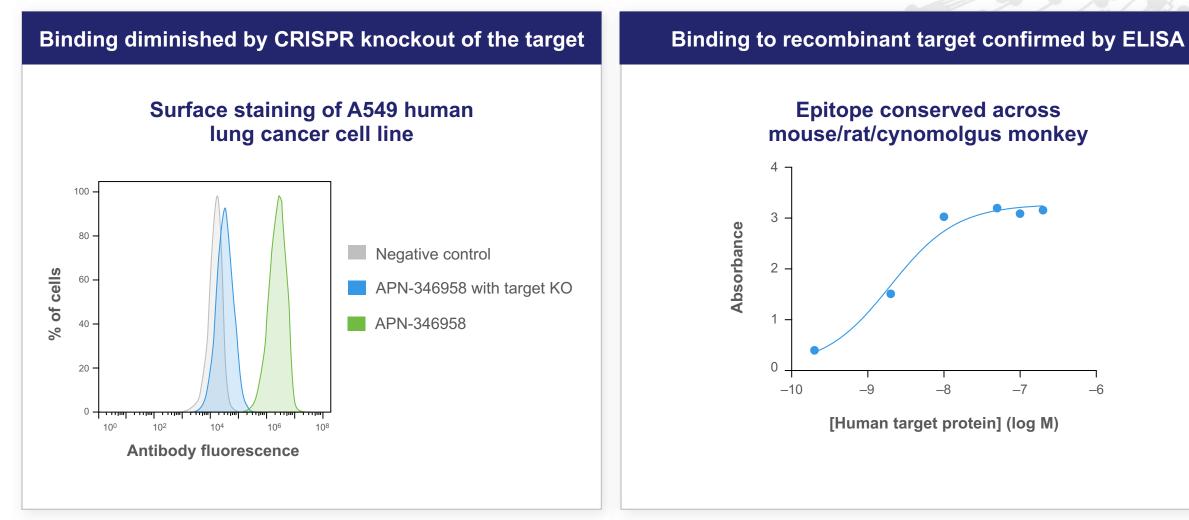


RNA, ribonucleic acid; snRNP, small nuclear ribonucleoprotein.

1. Ma J, et al. Clin Exp Immunol. 1993; 93:396–404; 2. Okawa-Takatsuji M, et al. Clin Exp Immunol. 2001;126:345–354; 3. Jordan P, et al. Mol Biol Reports. 1996;22:63–66.



## APN-346958 Binds the Surface of Human Tumor Cell Lines

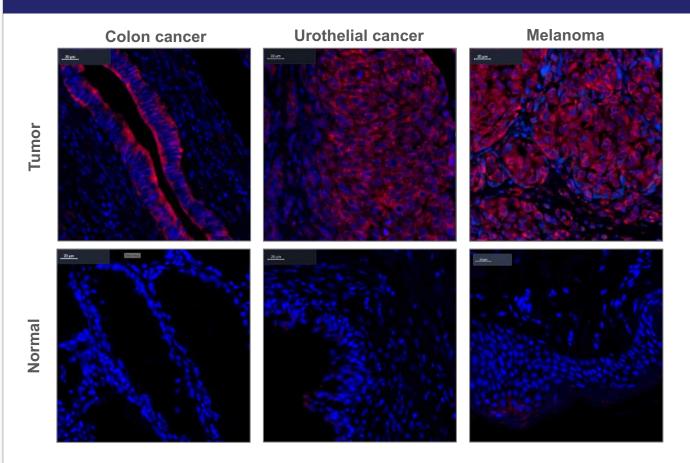


CRISPR, clustered regularly interspaced short palindromic repeats; ELISA, enzyme-linked immunosorbent assay.

# APN-346958 Pilot Survey Reveals Marked Prevalence in Multiple Cancer Types



#### Robust and tumor-selective signal observed in ≥50% of six tumor types



Indication	Percent reactive	Total cores scored
Colorectal cancer	75%	20
Thyroid cancer	68%	19
Head & neck cancer	67%	18
Urothelial cancer	63%	16
Melanoma	54%	13
Brain cancer	50%	20
NSCLC	42%	19
Cervical cancer	42%	19
Ovarian cancer	40%	15

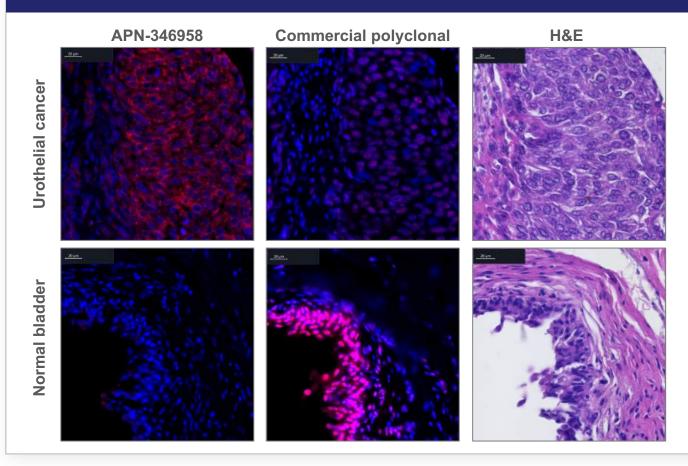
### Only faint-to-moderate cytoplasmic immunoreactivity observed in normal human tissues

NSCLC, non-small cell lung cancer.

APN-346958 May Recognize a Novel Tumor-associated Form of the Target Across Multiple Tumor Types



#### APN-346958 reactivity apparent in malignant cells *but not* stroma or normal tissues



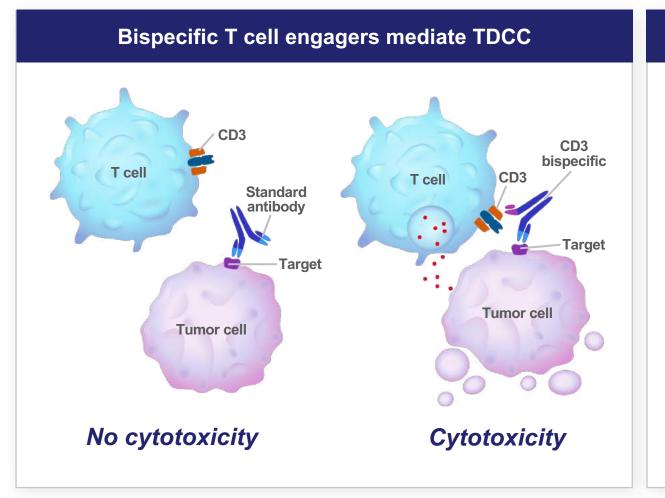
## APN-346958 compared to commercial polyclonal against target

- Differences observed across multiple tumor types
- Commercial polyclonal
  - Binds tumor **and** normal tissues
  - Has reactivity localized to the nucleus

H&E, hematoxylin and eosin; pAb, polyclonal antibody.

## Xencor and Atreca Collaborating to Discover and Develop Novel CD3-Engagers





#### **Collaboration highlights**

#### **Atreca brings:**

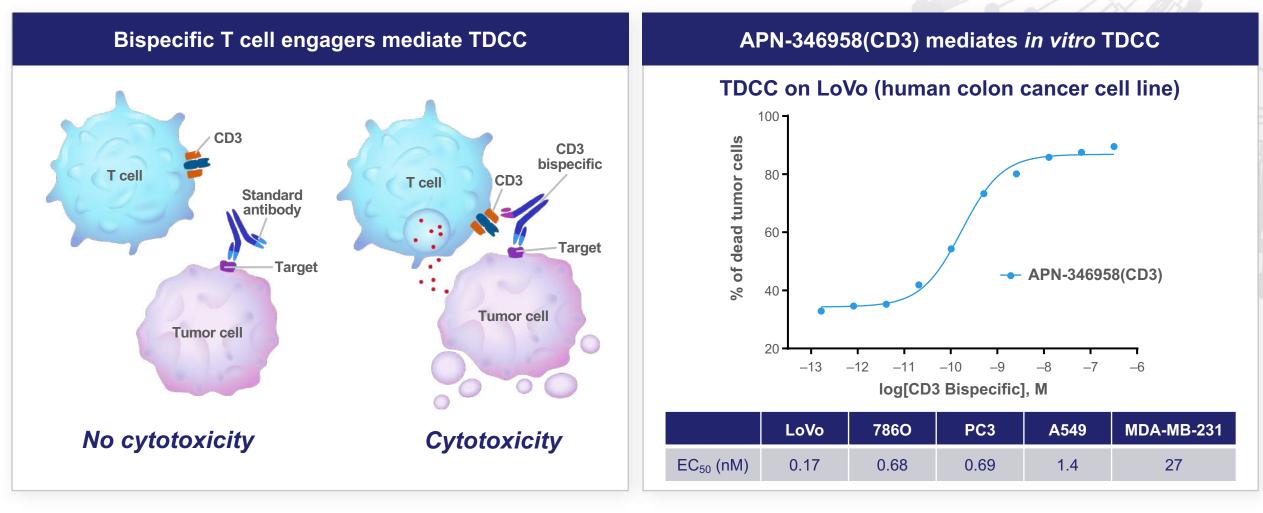
- Novel tumor-selective antibodies
- Target ID and epitope ID
- Antibody optimization

#### Xencor brings:

- Leadership in taking CD3-engagers from engineering through manufacturing and clinical development
- XmAb<sup>®</sup> bispecific Fc domain technology that retains fulllength antibody properties in bispecific antibody formats
- Tunable XmAb<sup>®</sup> 1+1 and 2+1 formats

### APN-346958(CD3) XmAb<sup>®</sup> Bispecific T Cell Engager Kills Tumor Cells *in Vitro*

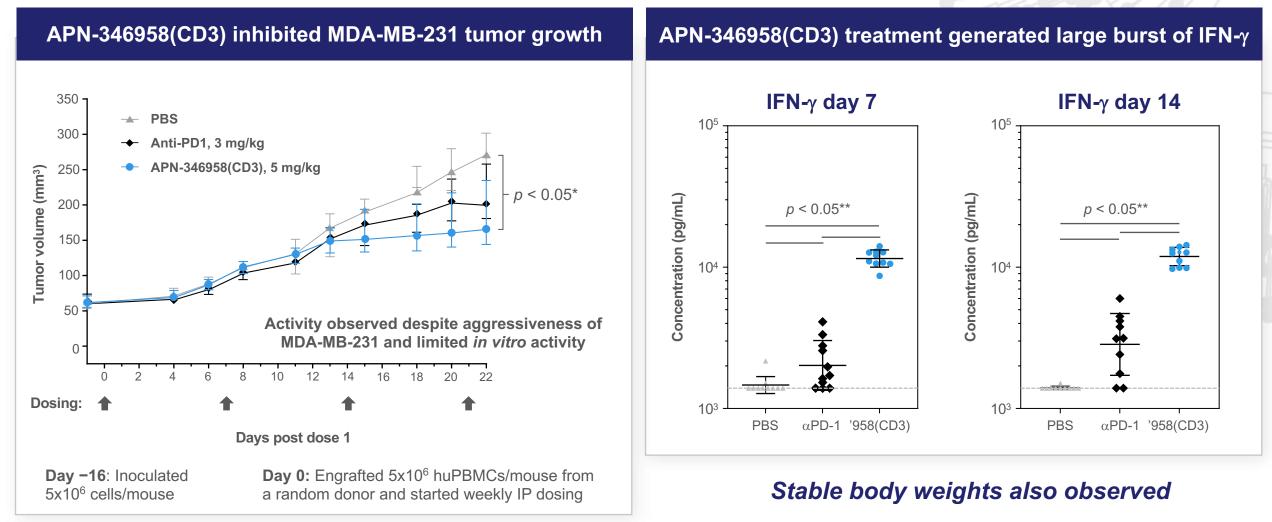




EC<sub>50</sub>, half maximal effective concentration; TDCC, T cell-dependent cellular cytotoxicity.

## APN-346958(CD3) Active *in Vivo* in Hard-to-Treat Humanized Mouse Tumor Model





\*One-sided Wilcoxon rank sum test for normalized area above the curve at Day 22. \*\*Two-sided unpaired t-test.

IFN-γ, interferon gamma; IP, intraperitoneal; PD-1, programmed cell death 1; PBS, phosphate-buffered saline; huPBMC, human peripheral blood mononuclear cell.



### APN-346958(CD3) Advancing Towards Candidate



- **APN-346958** binds a novel, tumor-selective target mislocated to cell surface
- Exhibits marked prevalence in six cancer types



- APN-346958 binds a species-conserved epitope
- May recognize a unique tumor-specific form of the target

Li Cher

- **APN-346958(CD3)** bispecific T cell engager:
- Active in vitro to kill cells
- Active *in vivo* to inhibit tumor growth



Lead optimization underway

- Leveraging yeast-display platform
- Evaluating tunable aspects of format (valency & CD3 potency)

## Lead Stage IL-15SA Fusion Program: APN-541885 (Lead)

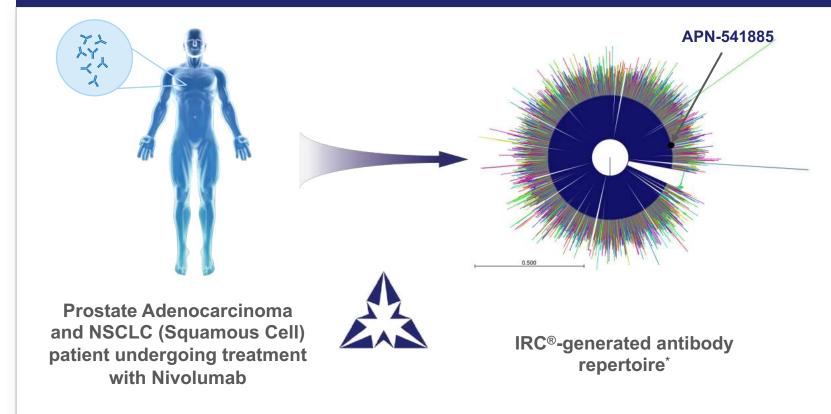
Amy Manning-Bog, PhD

VP, Translational Sciences



# APN-541885: An Antibody Targeting an Oncofetal Antigen

Lead antibody APN-541885 discovered via the Atreca platform



### Lead highlights

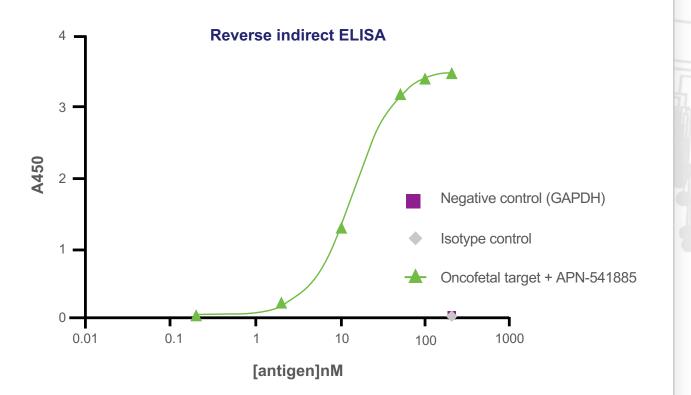
- Identified from sample collected post-nivolumab treatment
- APN-541885 derived from a persistent and expanded lineage
- APN-541885 selectively binds non-autologous human tumor tissue
- APN-541885 selectively binds human tumor cell lines
- No high-risk sequence-based liabilities



## APN-541885 Target Is a Well-described Oncofetal Protein

Target confirmed by ELISA

- Oncofetal proteins are expressed during development and only in tumors in adults
- Expression of APN-541885 target described in several cancers including melanoma, adenocarcinomas, squamous cell carcinomas, and hematological cancers
- Higher levels of APN-541885 target in tumor and circulation linked to worse survival



## APN-541885 Demonstrates Tumor-selective Binding Across Multiple Cancer Types



#### Robust APN-541885 reactivity apparent in malignant cells *but not* stroma or normal tissues

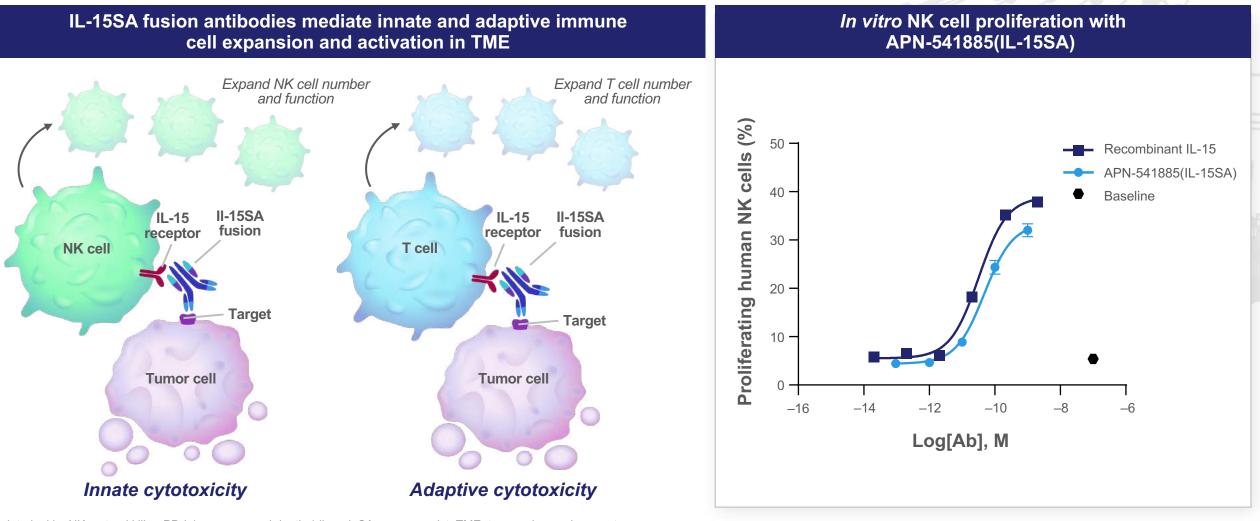
	NSCLC	Head and neck cancer	Esophageal cancer		Percent	Total cores	
		MARKAN A		Indication	reactive	scored	
Tumor			33 ye alter	NSCLC	68%	19	
			1. 18 P all	Thyroid cancer	67%	15	
				Cervical cancer	60%	15	
				Testicular cancer	59%	17	
Normal				Head and neck cancer	56%	16	
			1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1	Esophageal cancer	53%	15	
				Ovarian cancer	43%	14	
			Sal 180	Urothelial cancer	38%	13	
			10.50 Ca	Renal cancer	29%	14	

Minimal reactivity detected across normal human tissues with no membrane signal apparent

NSCLC, non-small cell lung cancer.

### APN-541885(IL-15SA) Promotes NK Cell Proliferation in Vitro

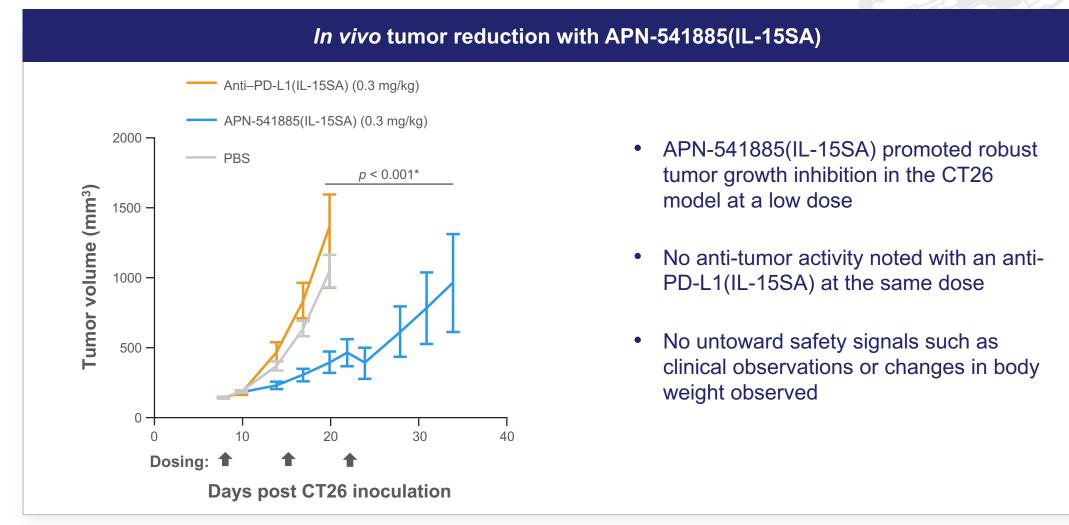




IL, interleukin; NK, natural killer; PD-L1, programmed death-1 ligand; SA, superagonist; TME, tumor microenvironment.

### APN-541885(IL-15SA) Shows Enhanced Anti-Tumor Activity *in Vivo* Compared to Anti-PD-L1(IL-15SA)



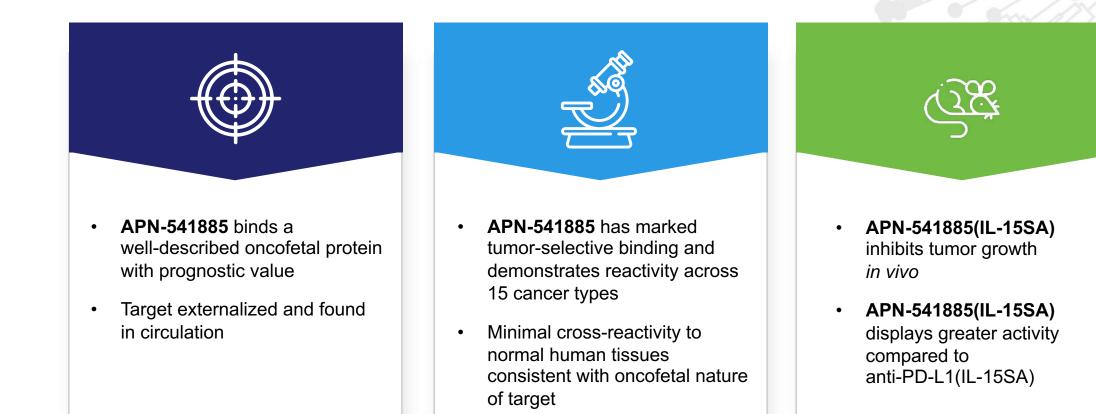


\*One-sided Wilcoxon rank sum test for normalized area above the curve at end of study for APN-541885(IL-15SA) vs Anti-PD-L1(IL-15SA).

IL, interleukin; PBS, phosphate-buffered saline; PD-L1, programmed death-1 ligand; SA, superagonist.

# Summary: APN-541885(IL-15SA) Profile Supports Advancement





# Business Development, Summary and Next Steps

John Orwin President and CEO



### Atreca's Pipeline

Candidate / Lead	Target	Format / MOA	Lead	Candidate / Preclinical	Phase 1	Phase 2	Weaponization Tech
NCOLOGY							
ATRC-101	Novel RNP Complex	IgG Antibody w/ Driver Antigen Engagement		0 0 0 0 0 0			
ATRC-301	EphA2	ADC (Cytotoxic)					<b>zyme</b> works
APN-122597	(novel epitope)	T Cell Engagement (via CD3)					
APN-497444	Glycan (tumor-specific)	ADC (Cytotoxic)		0 0 0 0 0 0 0 0 0 0 0 0			<b>zyme</b> works
APN-959038	Transmembrane protein (novel epitope)	ADC (Cytotoxic)		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			<b>zyme</b> works
APN-346958	RNA-binding protein	T Cell Engagement (via CD3)		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			Xencor
APN-541885	Oncofetal protein	NK & T Cell Engagement (via IL-15SA)		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
NFECTIOUS DISEASES							
ATRC-501 / MAM01 (Malaria)	<i>P. falciparum</i> Circumsporozoite Protein	IgG antibody					
APN-850271 / APN-906072 (COVID-19)	SARS-CoV-2 Spike Protein	IgG antibody					

ADC, antibody-drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2; IgG, immunoglobulin G; IL, interleukin; MOA, mechanism of action; NK, natural killer; RNA, ribonucleic acid; RNP, ribonucleoprotein; SA, superagonist; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### Partnering with World Leaders to Access Technologies for Atreca Antibody Weaponization



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

- Atreca provides antibodies against novel targets from which Xencor engineers 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 partner may pursue up to two programs independently with royalties payable on net sales



- Atreca's novel antibodies will be conjugated using ZymeLink<sup>™</sup>, **Zymeworks**' suite of proprietary cytotoxins, stable linkers, and conjugation technologies
  - Two-year Research Term for **Atreca** to evaluate antibodies as ADC's using ZymeLink<sup>™</sup> with the option for a 3rd year
  - Atreca can acquire up to 3 commercial licenses during the Research Term to develop 3 unique ADC programs

Existing agreements designed to facilitate further potential development and commercial partnerships

**Xencor** 

zymeworks

# Summary



Platform	<ul> <li>Atreca's drug discovery approach and platform validated by ATRC-101 clinical data</li> <li>Atreca platform continues to evolve and is delivering a robust pipeline</li> </ul>
ATRC-301	<ul> <li>ADC targeting EphA2 declared as clinical candidate</li> <li>Enabled by newly announced licensing agreement with Zymeworks</li> <li>Demonstrates potent anti-tumor activity <i>in vivo</i></li> <li>Differentiated from previous and current clinical-stage programs</li> </ul>
Pipeline	<ul> <li>Four additional lead-stage oncology programs advancing</li> <li>Lead antibodies bind novel tumor targets that vary in molecular class</li> <li>All programs have positive <i>in vivo</i> data</li> </ul>

ADC, antibody-drug conjugate; EphA2, erythropoietin-producing hepatocellular receptor A2.

## Financial/IP Overview



### **Financial Overview**

- \$125M equity financing completed in July 2020
- Current capital expected to be adequate to fund operations through 1H23
- Cash, cash equivalents & investments of \$148.1M as of December 31, 2021

### **Intellectual Property**

- Patents issued in multiple jurisdictions, including a granted US patent, covering critical aspects of Atreca's Immune Repertoire Capture<sup>®</sup> (IRC<sup>®</sup>) technology and platform exclusively licensed to Atreca
- Patent applications covering ATRC-101 and related antibodies pending worldwide
- Patent application covering ATRC-301 and related antibodies filed internationally
- US provisional applications filed covering pipeline assets



## Next Steps and Upcoming Milestones



ADC, antibody-drug conjugate; GLP, good laboratory practices; IND, investigational new drug; NHP, non-human primates.



# Q&A