

1 April 2021

---

# Aptevo Therapeutics

**A Leading Bispecific Antibody Company**

**NASDAQ: APVO**

# Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact, including statements regarding our financial guidance, product portfolio, product sales, capabilities, potential partnerships and collaborations, the ability of therapeutic candidates to function as designed in preclinical and clinical development, the continued advancement of product candidates in preclinical development and clinical trials, our goals and milestones, our expectations regarding the size of the patient populations for our therapeutic product candidates if approved for commercial use, our expectations regarding the safety and effectiveness of our ADAPTIR and ADAPTIR-FLEX platform technologies and our therapeutic product candidates, our ability to obtain regulatory approval for our therapeutic product candidates, our choice of funding sources and our ability to obtain non-dilutive funding, our expectations of future warrant exercises and the resulting impact to our cash position as a result thereof, the monetization of RUXIENCE and IXINITY payment streams, and any other statements containing the words “believes”, “expects”, “anticipates”, “intends”, “plans”, “forecasts”, “estimates” and similar expressions in conjunction with, among other things, discussions of financial performance or financial condition, growth strategy, product sales, manufacturing capabilities, product development, regulatory approvals or expenditures are forward-looking statements. These forward-looking statements are based on our current intentions, beliefs and expectations regarding future events. We cannot guarantee that any forward-looking statement will be accurate. Investors should realize that if underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could differ materially from our expectations. Investors are, therefore, cautioned not to place undue reliance on any forward-looking statement. Any forward-looking statement speaks only as of the date of this presentation, and, except as required by law, we do not undertake to update any forward-looking statement to reflect new information, events or circumstances.

There are a number of important factors that could cause Aptevo's actual results to differ materially from those indicated by such forward-looking statements, including possible negative effects on Aptevo's business operations, assets or financial results as a result of the separation; a deterioration in the business or prospects of Aptevo; adverse developments in Aptevo's customer-base or markets; our ability to enter into and maintain selective collaboration and partnership arrangements; the timing of and our ability to achieve milestones in collaboration and partnership contracts; our ability and the ability of our contractors and suppliers to maintain compliance with cGMP and other regulatory obligations; the results of regulatory inspections; the rate and degree of market acceptance and clinical utility of our products; the success of our ongoing and planned development programs; the timing of and our ability to obtain and maintain regulatory approvals for our therapeutic product candidates; and our commercialization, marketing and manufacturing capabilities and strategy and changes in regulatory, social and political conditions. Additional risks and factors that may affect results are set forth in our filings with the Securities and Exchange Commission (the SEC), including Aptevo's most recent Annual Report on Form 10-K, as filed on March 25, 2020, and its subsequent reports on Form 10-Q and current reports on Form 8-K.

The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from our expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in our periodic reports filed with the SEC, when evaluating our forward-looking statements.

Aptevo™, ADAPTIR™ and any and all Aptevo Therapeutics Inc. brand, product, service, and feature names, logos, and slogans are trademarks or registered trademarks of Aptevo Therapeutics Inc. or its subsidiaries in the United States or other countries. All rights reserved.

# Aptevo at a Glance (NASDAQ: APVO)

---

- Clinical-stage immunotherapy company
- Differentiated bispecific and multi-specific antibody platform technologies  
ADAPTIR™ and ADAPTIR-FLEX™
  - Enables generation of novel candidates designed for multiple MOAs
  - Utilizes best structure to fit desired biology, specificity and affinity
- Broad preclinical/clinical portfolio - multiple novel candidates in development
  - APVO436 – AML and MDS
  - APVO436 – Demonstrated clinical activity, reported two of nine patients achieved complete remission in cohort 6; one CR progressed, one patient no longer has a CR, but remains on drug <sup>(1)</sup>
  - ALG.APV-527 – Multiple solid tumors expressing tumor antigen 5T4
  - APVO603 – Multiple solid tumors
  - APVO442 – Affinity-optimized anti-CD3 for improved biodistribution to prostate tumors
- Market capital: ~\$134 million <sup>(2)</sup>
- Cash and investments: ~\$43 <sup>(3)</sup> million

(1) Preliminary data as of March 31, 2021

(2) As of end of day March 31, 2021

(3) As at December 31, 2020

# Experienced Leadership Team

## Senior Management

### **Marvin White – President & CEO**

Emergent Director; Former CFO, St. Vincent's Health;  
Former Executive Director & CFO, Lilly USA

### **Jeff Lamothe – SVP, CFO**

Former Emergent VP, Finance; Former CFO, Cangene Corporation

### **Jane Gross, Ph.D. – SVP, CSO**

Former Emergent VP, Research/Non-Clinical Development;  
Former VP Immunology Research ZymoGenetics Inc.

### **Scott Stromatt, M.D. – CMO\***

Former Emergent SVP, CMO; Former CMO, Trubion

### **Heather Boussois, Acting General Counsel**

Former Emergent Assistant General Counsel and Head of Intellectual Property.

### **Censia Pottorf – VP, Human Resources**

Former Head of HR at Sweetlabs, Inc., HR at GreatCall, Inc.

## Board of Directors

### **Marvin White**

Emergent Director; Former CFO, St. Vincent's Health;  
Former Executive Director & CFO, Lilly USA

### **Fuad El-Hibri**

Founder, Executive Chairman, Emergent BioSolutions

### **Daniel Abdun-Nabi**

Former President & CEO, COO, Emergent BioSolutions,  
Former General Counsel, IGEN International, Inc.

### **Grady Grant, III**

Former Vice President of Sales, Tissue Tech Limited;  
Former Reckitt Benckiser Group; Former Eli Lilly & Co.

### **Zsolt Harsanyi, Ph.D.**

N-Gene Research Labs; Exponential Biotherapies;  
Porton Int'l

### **Barbara Lopez Kunz**

DIA; Battelle; Thermo Fisher Scientific; ICI/Uniqema

### **John Niederhuber, M.D.**

Inova Translational Medicine Institute; National Cancer Institute; Johns Hopkins University

**Deep R&D, Manufacturing, Commercial and Financial  
Expertise and Experience**

\*Dr. Stromatt is a consultant to the company.

# Our Strategy

---

- 1** Develop and advance novel immuno-oncology product candidates using the **ADAPTIR** and **ADAPTIR-FLEX** platform technologies
- 2** Expand collaborations and partnerships
- 3** Maximize non-dilutive funding sources to support future capital requirements



# APTEVO – 2021 YTD Financial Highlights

- Sold RUXIENCE® Royalty Stream (Pfizer rituximab biosimilar) to an entity managed by HealthCare Royalty Management, LLC (“HCR”) effective March 30, 2021 for \$35 million up front, plus milestones of up to \$32.5 million. Additionally, once HCR reaches aggregate royalty payments totaling 190% of the upfront amount plus any milestones paid to Aptevo, Aptevo will be entitled to receive 50% of any royalty payments made by Pfizer thereafter. The milestones may be earned based on net sale performance of RUXIENCE as follows:

Year	Total Maximum Milestones earnable per year (millions)
2021	\$10
2022	\$12.5
2023	\$10

- Utilized \$10 million of proceeds received from the RUXIENCE royalty sale to pay down outstanding principal on the MidCap Financial (“MidCap”) term loan, leaving \$15 million of principal outstanding.
- After receipt of the upfront payment from HCR and payment to MidCap, the Company’s cash runway is extended into Q2 2022. If earned, collection of the above milestones will provide further non-dilutive funding to the Company.

# Projected Milestones – Within Next 12-18 Months


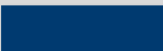
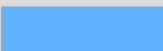
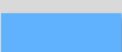


## Development/Clinical

- Complete dosing in ongoing APVO436 Phase 1a clinical trial
- Advance ALG.APV-527 into clinical development with Alligator Bioscience in solid tumors expressing 5T4. First-in-human dosing planned for Q4 2021
- APVO603; initiating IND-enabling studies and CMC activities to support IND submission in 2022.
- Advance APVO442 in preclinical development
- Explore additional candidate(s) using ADAPTIR and/or ADAPTIR-FLEX platform technologies

## Operational/Financial

- Continue current and initiate future partnering discussions around product candidates as well as ADAPTIR and ADAPTIR-FLEX platform technologies
- Collect quarterly IXINITY® royalties
- Collect potential HCR milestone payments, based on RUXIENCE net sales

# Aptevo Pipeline: Robust and Diversified Product Candidate Portfolio

Product/ Candidate Target	Technology	Potential Indications	Pre- Clinical	Clinical Development Stage			Marketed	Milestones/Highlights
				Phase I	Phase II	Phase III		
APVO436 CD3/CD123	Redirected T-Cell Cytotoxicity (RTCC)	AML/MDS (R/R)						Phase 1/1b study ongoing; 2 CR reported in cohort 6
APVO436 CD3/CD123	Redirected T-Cell Cytotoxicity	AML front- line setting						Selected for inclusion in groundbreaking 'BEAT AML® Master Clinical Trial' spearheaded by LLS
ALG.APV-527* 4-1BB/5T4	T-Cell Co- Stimulation	Multiple Solid Tumors						Advancing into clinical development with Alligator Bioscience in 2021.
APVO603 4-1BB/OX40	Dual T-Cell Co-stimulation	Multiple Solid Tumors						Unique asset for use in multiple solid tumors; Advancing lead candidate
APVO442 PSMA/CD3	Redirected T-Cell Cytotoxicity	CRPC						Low affinity CD3 Advancing lead candidate
Multiple Candidates	Bispecific RTCC and New MOA	Hematologic and Solid Tumors						Advancing new candidates that modulate the immune system

\* Partnered with Alligator Bioscience



# ADAPTIR – A Differentiated, Homodimer Bispecific Technology

## Modular and Flexible

- Monospecific and bispecific formats
- Reproducible generation of homodimeric bispecifics with desired mechanism of action and potency

## Designed For Multiple Mechanisms of Action

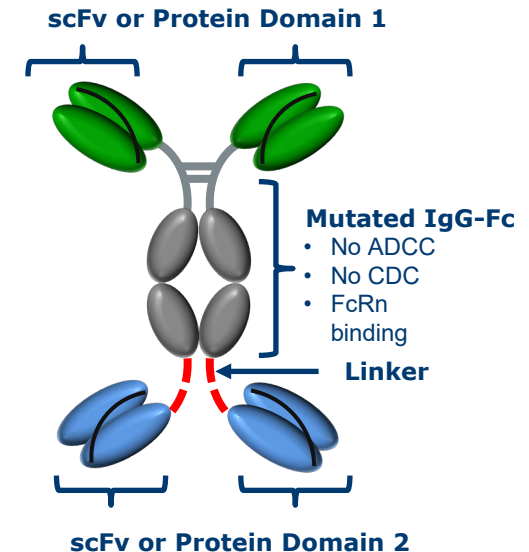
- Redirected T-Cell Cytotoxicity (RTCC)
- Tumor directed co-stimulation of immune receptors to re-engage immune response
- Dual receptor targeting that can stimulate or inhibit immune responses

## Excellent Manufacturability Characteristics

- Antibody backbone increases stability
- Designed to minimize proteolytic cleavage and post-translational modifications
- Standard manufacturing process with high yields and purity

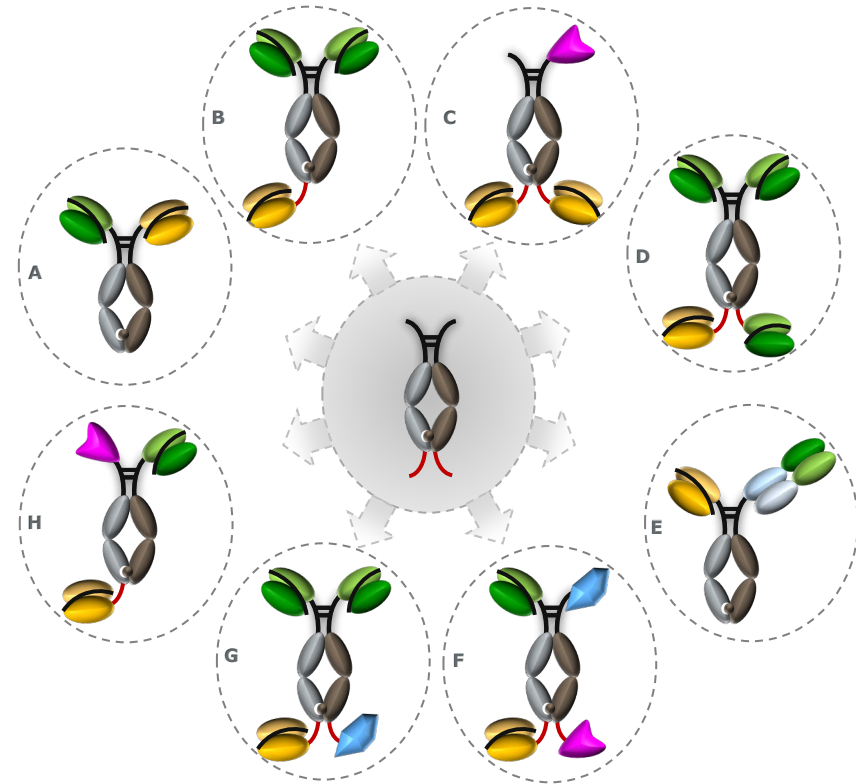
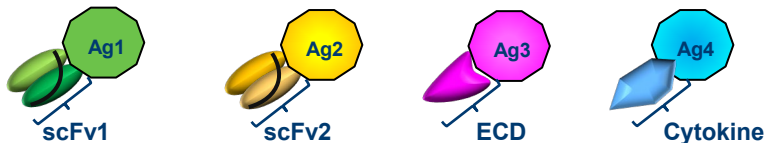
## Antibody-like Half-Life

- Half-life up to 12.5 days in rodents



# ADAPTIR-FLEX: Heterodimer Platform Technology Overview

- Heterodimer technology designed to produce bispecific and multispecific drug candidates
- Leverages IgG1 Fc with “Knob in Hole” to assemble two different protein chains
- Enables binding, activating or blocking of up to four different targets
- Ability to mutate to eliminate Fc effector function
- Shares key features with ADAPTIR technology
  - IgG1 backbone and Fc mutations
  - Linkers



scFv domains from IgGs, extracellular domains (ECD) and cytokines with different specificities and functional properties

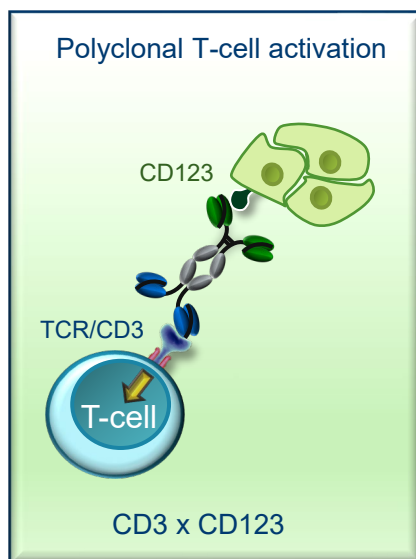
# ADAPTIR and ADAPTIR-FLEX Platform Technologies Aptevo For Design of Development of Novel Therapeutics

---

- ADAPTIR Bispecifics are based on a ***robust platform technology*** with potential advantages over other platforms
  - Increased stability and half-life
  - Antibody-like manufacturing
  - Ease of transfer and manufacturing at CMOs
- ADAPTIR and ADAPTIR-FLEX T-cell engagers are based on a ***unique and proprietary anti-CD3***
  - Demonstrated potent tumor lysis *in vitro* and *in vivo* (preclinical models)
  - Reduced cytokine release in preclinical studies may improve tolerability in a clinical setting
- ADAPTIR and ADAPTIR-FLEX can be used to design ***therapeutics with multiple MOAs***
  - Generation of multiple anti-CD3 based T-cell engagers for hematologic and solid tumors
  - Utilization of TNFR superfamily members or other activating receptors (e.g.)
  - Targeting cytokines to modulate the immune system for multiple indications

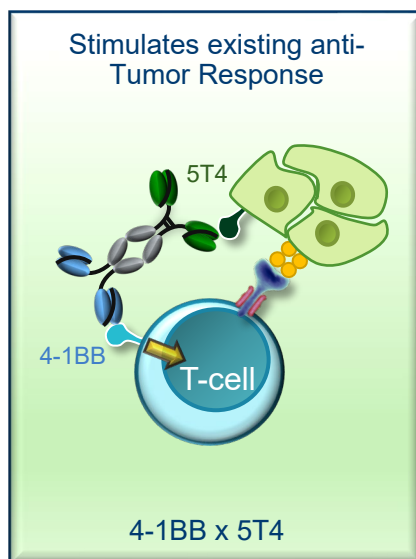
# ADAPTIR And ADAPTIR-FLEX: Multiple Candidates Designed for Different MOAs in Current Pipeline

*CD3 T-Cell Engager  
Targeting a Tumor Antigen*



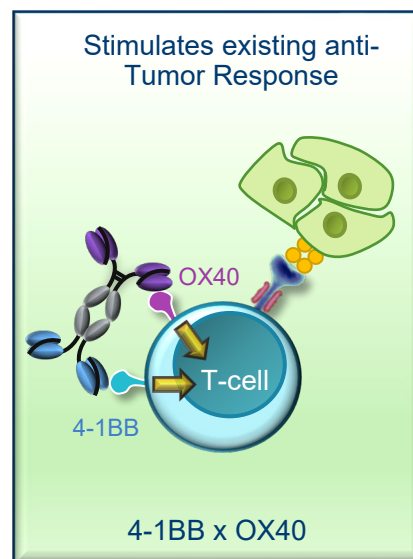
**APVO436**

*Tumor Antigen Dependent  
4-1BB Co-stimulator*



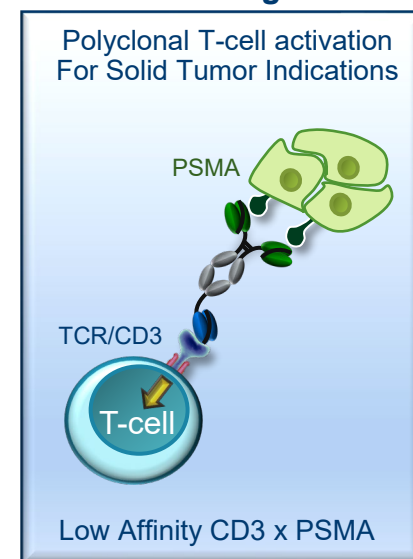
**ALG.APV-527**

*Dual TNFR Co-stimulator  
Targeting 4-1BB/OX40*



**APVO603**

*Low Affinity CD3 T-Cell  
Engager Targeting a Solid  
Tumor Antigen*

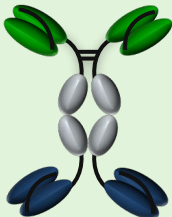


**APVO442**

**ADAPTIR**

**ADAPTIR-FLEX**

# APVO436 – A Novel Immunotherapy Candidate for AML

<b>CANDIDATE</b>	 <p>αCD123 scFv</p> <p>αCD3 scFv</p>
<b>OPPORTUNITY</b>	<ul style="list-style-type: none"> <li>• ADAPTIR (CD123 x CD3) T-cell engager</li> <li>• Preclinical studies showed key differentiation from another bispecific format*</li> </ul>
<b>TARGET/MOA</b>	<ul style="list-style-type: none"> <li>• CD123 - compelling target for AML due to its overexpression on leukemic stem cells and AML blasts; Designed to engage T-cells via binding to CD3 to specifically kill tumor cells expressing CD123</li> </ul>
<b>POTENTIAL INDICATIONS</b>	<ul style="list-style-type: none"> <li>• AML, MDS, ALL, hairy cell leukemia, myelodysplastic syndrome</li> <li>• Strong unmet need for safe and effective new therapies</li> </ul>
<b>DEVELOPMENT STAGE</b>	<ul style="list-style-type: none"> <li>• Phase 1 study dose escalation in R/R AML and MDS ongoing</li> <li>• Orphan drug designation granted by FDA for AML</li> <li>• Selected for inclusion in groundbreaking BEAT AML Master Clinical Trial; which will evaluate APVO436 in front-line AML setting</li> </ul>
<b>PARTNERSHIP STATUS</b>	<ul style="list-style-type: none"> <li>• Wholly-owned by Aptevo</li> </ul>

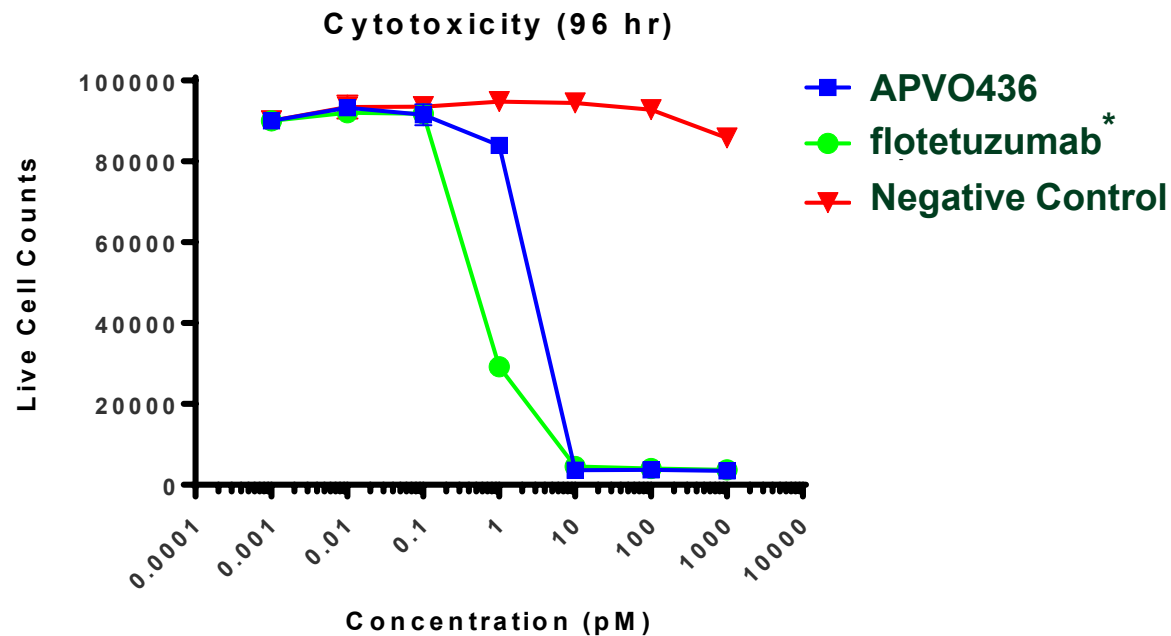
\*Aptevo-generated version of Macrogenics' CD123 x CD3 dual-affinity re-targeting (D.A.R.T) molecule, MGD006

# AML / MDS Opportunity\*

- AML: 21,000 new cases/year in U.S. 10,500 deaths/year in U.S.
  - Average age 67 years / 5-year survival 26%
- MDS: 10,000 – 20,000 new cases/year in U.S.
  - 1 in 3 patients with MDS will progress to have AML
- Front-line treatment is chemotherapy
  - Standard therapy = “7+3”; cytarabine and daunorubicin for induction over 1-2 mos
  - Consolidation therapy (chemotherapy, radiation, stem cell transplant)
- Strong unmet need for novel therapies that improve outcomes and survival
  - Elderly, newly diagnosed, high-risk, relapsed/refractory patients
- CD123 broadly expressed in AML blasts and on leukemic stem cells
  - Numerous novel targeted agents in development



# ADAPTIR T-Cell Engager Candidate APVO436 Induced Similar T-cell Cytotoxicity Compared to Another Bispecific Format in *In Vitro* Studies<sup>+</sup>

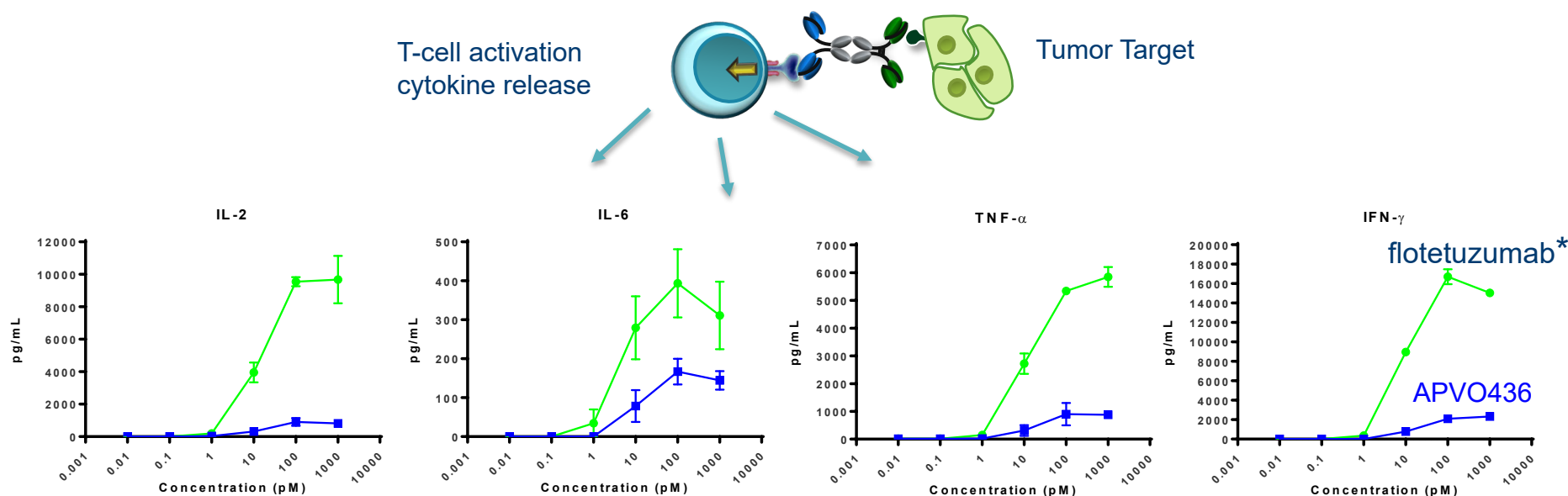


+ AACR 2018 Poster: APVO436, a Bispecific anti-CD123 x anti-CD3 ADAPTIR Molecule for Redirected T-cell Cytotoxicity, Induces Potent T-cell Activation, Proliferation and Cytotoxicity with Limited Cytokine Release

\* Aptevo-generated version of flotetuzumab used in head-to-head studies

# ADAPTIR T-Cell Engager Candidate APVO436 Induced Lower Levels of Cytokines Than Another Bispecific Format in *In Vitro* Studies

APVO436 generated lower levels of cytokines when tumor antigen present compared to another bispecific format targeting the same tumor antigen in *in vitro* studies<sup>+</sup>



Cytokines measured after 20 hr stimulation of T-cells with ADAPTIR and tumor cells

<sup>+</sup> AACR 2018 Poster: APVO436, a Bispecific anti-CD123 x anti-CD3 ADAPTIR Molecule for Redirected T-cell Cytotoxicity, Induces Potent T-cell Activation, Proliferation and Cytotoxicity with Limited Cytokine Release

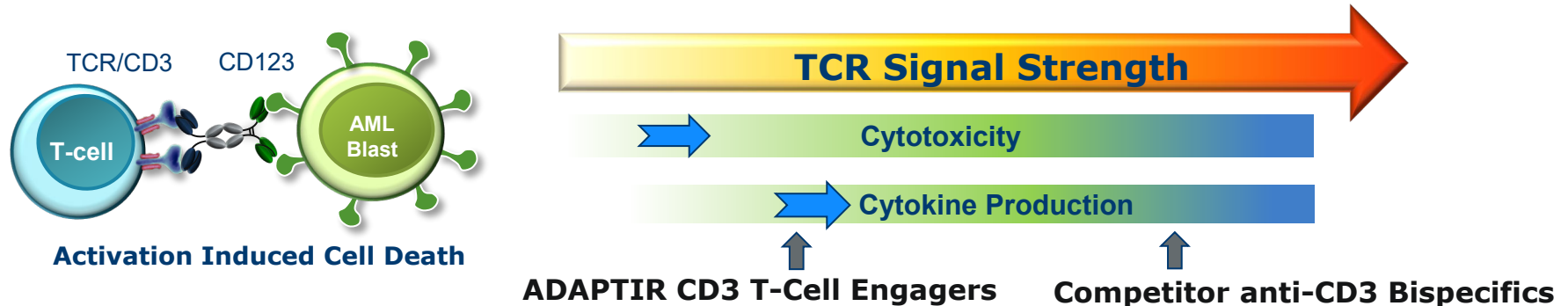
\* Aptevo-generated version of flotetuzumab used in head-to-head studies



# Unique ADAPTIR T-Cell Engagers

## Functional Characteristics in Preclinical Studies

**Theory: Lower Levels of TCR stimulation needed for Cytotoxicity vs Cytokine Production<sup>2</sup>**



- ADAPTIR CD3 bispecifics induce robust target lysis and T-cell activation, but with lower cytokine release in preclinical studies
- APVO436 (anti-CD123 x anti-CD3) demonstrated reduced cytokine release *in vitro* with equivalent potency to kill tumor target expressing CD123
  - Compared to a competitor candidate generated at Aptevo

1. Same amino acid sequence to MGD006 CD3xCD123 D.A.R.T. ([Blood](#). 2016 Jan 7; 127(1): 122–131)  
2. Faurodi et al *PNAS* 2013; 100:14145

# APVO436 Key Potential Differentiation From Other Bispecifics Targeting CD123 and CD3

## APVO436 – Potential Key Differentiators

<b>Novel structure</b>	<ul style="list-style-type: none"><li>• Supports traditional antibody-like manufacturing processes</li><li>• Single gene construct and CHO production cell line</li></ul>
<b>Half-life</b>	<ul style="list-style-type: none"><li>• Half-life of 12.5 days in rodents and 4.5 days in NHPs</li><li>• Enables potential for improved dosing regime in clinic</li></ul>
<b>Cytokine release</b>	<ul style="list-style-type: none"><li>• <i>In vitro</i> data showed lower levels of cytokine release versus Aptevo-generated version of flotetuzumab in head-to-head studies<sup>+</sup></li><li>• Comparable <i>in vitro</i> tumor lysis and T-cell activation data compared to Aptevo-generated version of flotetuzumab in head-to-head studies<sup>+</sup></li><li>• Potential for superior safety profile and broader therapeutic window</li></ul>

<sup>+</sup>AACR 2018 Poster: APVO436, a Bispecific anti-CD123 x anti-CD3 ADAPTIR Molecule for Redirected T-cell Cytotoxicity, Induces Potent T-cell Activation, Proliferation and Cytotoxicity with Limited Cytokine Release

# APVO436 Clinical Development Program

## Phase 1a/1b Open-Label, Dose-Escalation Clinical Trial

<b>Study Design</b>	Phase 1a: Determine maximum tolerated dose and recommended dose for Phase 1b Phase 1b: Assess clinical activity at recommended dose
<b>Administration</b>	APVO intravenous (IV) dosing weekly for six 28-day cycles
<b>Subjects</b>	Phase 1a: up to 60 patients Phase 1b: up to 48 patients
<b>Status</b>	Complete Remission demonstrated in 2 patients (Cohort 6a and 6b). Demonstrated clinical activity, reported two of nine patients achieved complete remission in cohort 6; one CR progressed, one patient no longer has a CR, but remains on drug Dose escalation ongoing. 41 patients enrolled and treated to date. Enrolling in cohort 10 One DLT in 1 of 6 patients in cohort 4; no DLTs in cohorts 5 - 9

# APVO436 Selected for Inclusion in the Leukemia & Lymphoma Society 'Beat AML<sup>®</sup>' Master Clinical Trial'

---



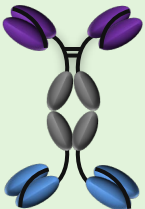
- Groundbreaking national clinical trial
- Spearheaded by the Leukemia & Lymphoma Society
- Evaluating novel AML and MDS immunotherapies
- 14 leading cancer centers including:
  - Memorial Sloan Kettering Cancer Center, The Ohio State University Comprehensive Cancer Center, Oregon Health and Science University Knight Cancer Institute and Mayo Clinic
- APVO436 selected for inclusion alongside industry leaders
  - Bristol-Myers Squibb (formerly Celgene) Alexion Pharmaceuticals, Gilead Sciences, Takeda Oncology, Agios Pharmaceuticals, Astellas Pharma and Boehringer Ingelheim as an Industry Participant
- APVO436 to be tested in combination with decitabine in newly diagnosed AML patients
- Anticipated benefits of participation in Beat AML<sup>®</sup> trial:
  - Provides access to leading national cancer centers
  - Evaluates APVO436 in a front-line AML treatment setting
  - Complements ongoing Phase 1a/1b study in relapsed/refractory AML

# APVO436 – Summary

---

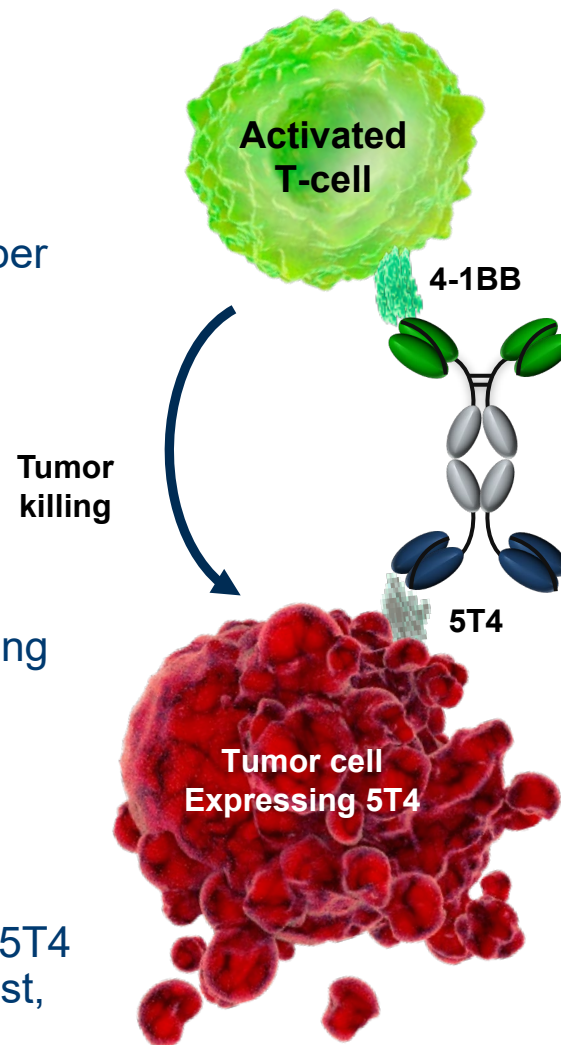
- A bispecific T-cell engager candidate designed to target CD123 x CD3
  - Designed to result in potent T-cell mediated killing of CD123+ tumors (no killing without target present)
  - Reduced cytokines observed in preclinical studies compared to Aptevo-generated version of flotetuzumab
  - Binding confirmed to cynomolgus monkey CD3 and CD123 ex-vivo
- Half-life of 12.5 days in rodents and 4.5 days in NHPs
- Preclinical *in vivo* proof-of-concept established in multiple xenograft tumor models
- High titer CHO cell clone production levels ~1.5 g/L
- Good manufacturability attributes
- Phase 1 dose-escalation ongoing in AML and MDS
  - Reported two complete remissions in cohort 6 in November 2020
  - Demonstrated clinical activity, reported two of nine patients achieved complete remission in cohort 6; one CR progressed, one patient no longer has a CR, but remains on drug
  - Currently enrolling in cohort 10
  - One DLT in 1 of 6 patients in cohort 4; no DLTs in cohorts 5 – 9
  - Received orphan drug designation from FDA for AML
- Selected for inclusion in groundbreaking ‘Beat AML® Master Clinical Trial’

# ALG.APV-527 – Broad Potential Therapeutic Opportunity in Solid Tumors

CANDIDATE	 <p><b>α4-1BB scFv</b></p> <p><b>α5T4 scFv</b></p>
OPPORTUNITY	<ul style="list-style-type: none"> <li>Designed to engage T-cells through co-stimulatory receptor 4-1BB</li> </ul>
TARGET/MOA	<ul style="list-style-type: none"> <li>Targets 4-1BB (co-stimulatory receptor) and 5T4 (tumor antigen)</li> <li>Designed to reactivate antigen-primed T-cells to specifically kill tumor cells; Designed to promote CD8 T-cell survival and effector function</li> </ul>
POTENTIAL INDICATIONS	<ul style="list-style-type: none"> <li>Multiple solid tumor indications: breast, cervical, non-small-cell-lung, prostate, renal, gastric, colorectal and bladder cancers</li> </ul>
DEVELOPMENT STAGE	<ul style="list-style-type: none"> <li>Advance into clinical development with Alligator Bioscience in solid tumors expressing 5T4. First-in-human dosing planned for Q4 2021</li> </ul>
PARTNERSHIP STATUS	<ul style="list-style-type: none"> <li>Joint 50/50 ownership &amp; co-development agreement with Alligator Bioscience</li> </ul>

# ALG.APV-527 Targeted Immunotherapeutic Bispecific Antibody Candidate Targeting 4-1BB x 5T4

- New MOA demonstrates ADAPTIR versatility
- Designed to simultaneously target
  - 4-1BB - costimulatory receptor, member of TNFR super family
  - 5T4 is a oncofetal tumor antigen
- Promising approach for targeted immunotherapy designed to:
  - Target T-cells previously activated by tumor antigen
  - Exert tumor-localized T-cell activation upon 5T4 binding
  - Not stimulate all (resting or naive) T-cells
- Potential Advantages:
  - Improved efficacy and safety (targeted therapy)
  - Opportunity to treat multiple solid tumors expressing 5T4 antigen (e.g. NSCLC, renal, pancreas, prostate, breast, ovarian, cervical)



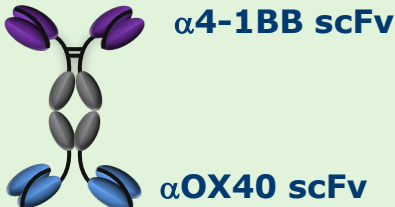
# ALG.APV-527 Summary

---

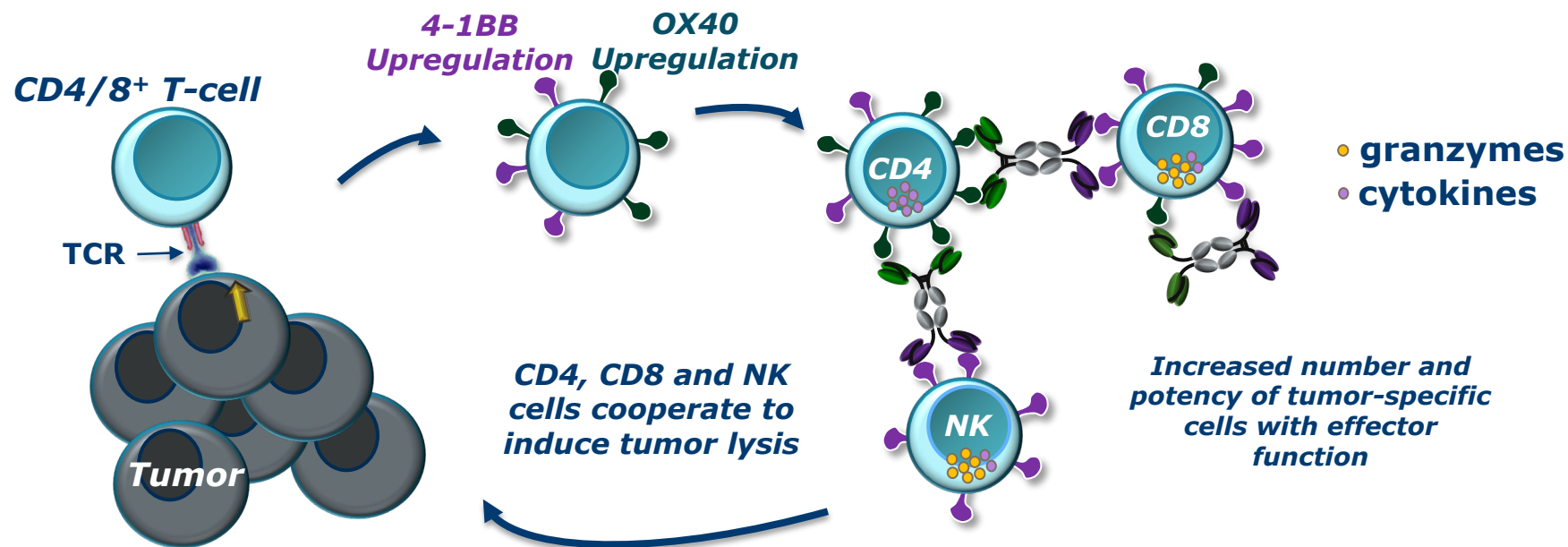
- Limited potential competition.
- Designed for 5T4-dependent tumor-directed T-cell activation to overcome dose-limiting toxicities seen with 4-1BB mAbs.
- Optimized in the ADAPTIR format for activity, solubility, stability and manufacturability properties.
- 5T4-dependent T-cell and NK-cell proliferation and activation, 5T4-driven tumor localization, and anti-tumor efficacy observed in preclinical studies.
- Advancing into clinical development with Alligator Biosciences in solid tumors expressing 5T4. First-in-human dosing planned for Q4 2021



# APVO603 – Dual Agonistic Bispecific Antibody Candidate

<b>CANDIDATE</b>	
<b>OPPORTUNITY</b>	<ul style="list-style-type: none"> <li>Designed to simultaneously target 4-1BB and OX40 both members of the TNF-receptor family</li> </ul>
<b>TARGET/MOA</b>	<ul style="list-style-type: none"> <li>Targets two costimulatory receptors 4-1BB and OX40</li> <li>Designed to provide synergistic co-stimulation of T-cells to potentially amplify the cytotoxic function of activated T-cells and NK cells; potential to promote more robust anti-tumor responses</li> </ul>
<b>POTENTIAL INDICATIONS</b>	<ul style="list-style-type: none"> <li>Multiple solid tumor indications; based on previous anti-tumor T-cell response</li> </ul>
<b>DEVELOPMENT STAGE</b>	<ul style="list-style-type: none"> <li>Preclinical proof of concept established</li> <li>IND-enabling and CMC activities underway; IND filing in 2022</li> </ul>
<b>PARTNERSHIP STATUS</b>	<ul style="list-style-type: none"> <li>Wholly-owned by Aptevo</li> </ul>

# Designed to Activate Multiple Immune Pathways to Increase Anti-Tumor Response and Reduce Toxicity\*



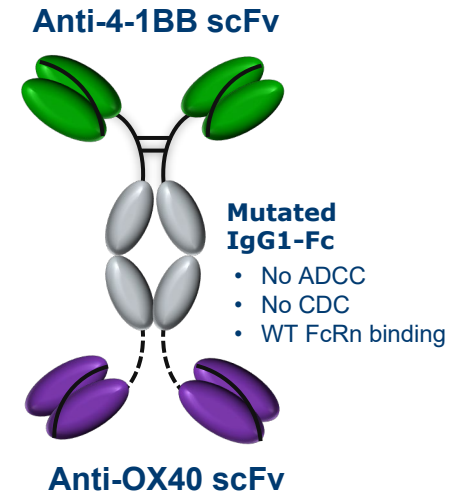
## Potential Key Advantages:

- Enhancement of pre-existing anti-tumor responses
- Enhancement of all effector lymphocyte populations: CD4, CD8 and NK cells
- Potential to reduce toxicities observed for competitor 4-1BB monospecific antibodies; APVO603 is designed to limit non-specific activation of lymphocytes

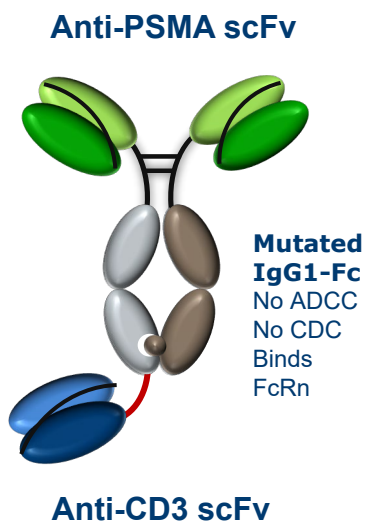
# APVO603 Summary

---

- APVO603 is a novel ADAPTIR bispecific with a unique mechanism of action that may boost natural anti-tumor responses by activating two different co-stimulatory receptors
- Application in multiple solid tumor indications to reinvigorate immune responses and enhance tumor rejection
- Preclinical studies demonstrate synergistic activation of CD4 and CD8 T cell and NK cell activation in addition to enhanced tumor cell lysis
- Lead candidate identified; CMC activities initiated
- Initiating IND-enabling studies and CMC activities to support IND submission in 2022



# APVO442 – Preclinical Program: A Novel Immunotherapy Designed for Prostate Cancer

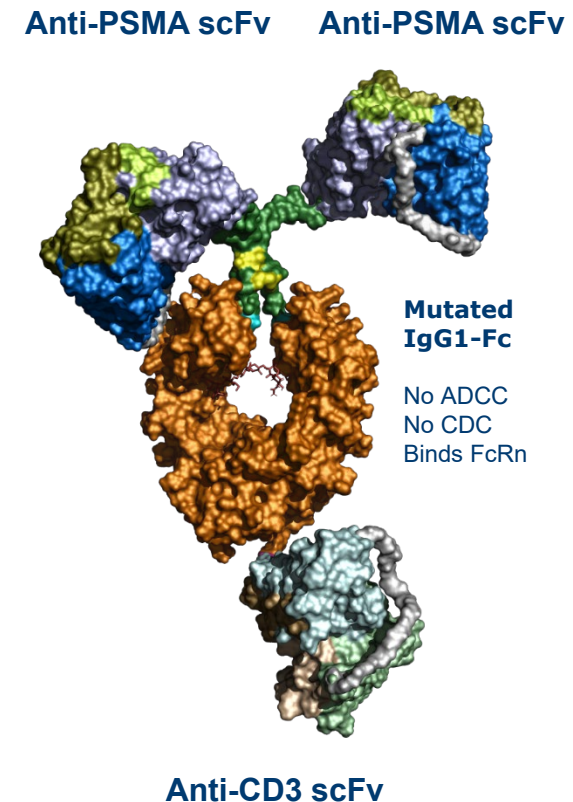


<b>THERAPEUTIC CANDIDATE</b>	<ul style="list-style-type: none"> <li>• <math>\alpha</math>PSMA x <math>\alpha</math>CD3 (low affinity) T-Cell Engager</li> </ul>
<b>TARGET/MOA</b>	<ul style="list-style-type: none"> <li>• Engages T cells via CD3 epsilon to lyse tumor cells expressing PSMA</li> <li>• Low-affinity CD3 reduces binding to circulating T cells</li> <li>• Designed to enable better biodistribution to solid tumors</li> <li>• Low levels of cytokines demonstrated in preclinical studies</li> </ul>
<b>POTENTIAL INDICATIONS</b>	<ul style="list-style-type: none"> <li>• Metastatic Castration-resistant prostate cancer and other PSMA(+) tumors</li> </ul>
<b>HALF-LIFE</b>	<ul style="list-style-type: none"> <li>• 9.3 days in mice</li> </ul>
<b>MANUFACTURABILITY</b>	<ul style="list-style-type: none"> <li>• Excellent manufacturability</li> <li>• Utilizes standard mAb production processes</li> </ul>
<b>DEVELOPMENT STAGE</b>	<ul style="list-style-type: none"> <li>• Lead candidate selected</li> <li>• Pre-clinical studies ongoing</li> </ul>

# Low Affinity Anti-CD3 Designed to Improve Solid Tumor Biodistribution

## APVO442 uses ADAPTIR-FLEX technology to achieve a “2+1” bispecific

- Bivalent, high affinity binding to PSMA
- Monovalent, low-affinity variant of anti-CD3 domain used in APVO436
  - Retains low cytokine release of previous anti-CD3 ADAPTIR candidates
  - Retains stability/manufacturability of previous candidates
- Optimized affinities designed to maximize distribution to prostate tumors
  - Minimize binding to circulating T cells
- Fc mutations to minimize Fc receptor and complement binding and activity
- Modular technology applicable to build CD3-engagers against other solid tumors



# APVO442 – Summary

---

## APVO442 based on ADAPTIR-FLEX Platform Technology

- Designed to minimize binding to circulating T cells, and maximize distribution to PSMA+ solid tumors
- Good manufacturability attributes

## Preclinical data demonstrating potent T-cell engager targeting PSMA and CD3

- Potent T-cell mediated killing of PSMA+ tumors *in vitro* and in a mouse model of disease
  - No killing without target present
- Reduced cytokines observed in preclinical studies compared to competitor molecule

## Antibody-like half-life in rodents (~9 days)

## Preclinical *in vivo* proof-of-concept established in C4-2B xenograft tumor models

# Why Aptevo?

---

- 1** Established leadership and capabilities in designing protein-based therapeutic candidates for cancer.
- 2** Proprietary, versatile, differentiated ADAPTIR and ADAPTIR-FLEX platform technologies that enable generation of new candidates in pipeline.
- 3** Pipeline of clinical and preclinical bispecific candidates advancing.
- 4** Portfolio with potential for multiple partnerships.
- 5** Cash runway into Q2 2022. Aptevo believes this is beyond the currently anticipated time required to achieve a potentially efficacious dose level in the APVO 436 Phase 1a/1b clinical trial.

---

# Aptevo Therapeutics

**Global Headquarters  
Aptevo Therapeutics  
2401 4th Avenue, Suite 1050  
Seattle, WA 98121  
Tel: 206-838-0500  
Fax: 206-838-0503  
Email: [ir@apvo.com](mailto:ir@apvo.com)**

**NASDAQ: APVO**