

6 June 2022

Aptevo Therapeutics

A Leading Bispecific Antibody Company

NASDAQ: APVO

Forward-Looking Statements



Safe Harbor Statement

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical fact, including, without limitation, Aptevo's expectations about the activity, efficacy and safety of its therapeutic candidates and potential use of any such candidates as therapeutics for treatment of disease, advancement of its clinical trials and its expectations regarding the effectiveness of its ADAPTIR and ADAPTIR-FLEX platforms, and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "optimism," "potential," "designed," "engineered," "breakthrough," "innovative," "innovation," "promising," "plans," "forecasts," "estimates," "will" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based on Aptevo's current intentions, beliefs, and expectations regarding future events. Aptevo 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 Aptevo's expectations. Investors are, therefore, cautioned not to place undue reliance on any forward-looking statement.

There are several important factors that could cause Aptevo's actual results to differ materially from those indicated by such forwardlooking statements, including a deterioration in Aptevo's business or prospects; adverse developments in clinical development, including unexpected safety issues observed during a clinical trial; adverse developments in the U.S. or global capital markets, credit markets or economies generally; and changes in regulatory, social, and political conditions. For instance, actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the uncertainties inherent in the initiation, enrollment and maintenance of patients, and completion of clinical trials, availability and timing of data from ongoing clinical trials, expectations for the timing and steps required in the regulatory review process, including our ability to obtain regulatory clearance to commence clinical trials, expectations for regulatory approvals, the impact of competitive products, actions of activist stockholders, our ability to enter into agreements with strategic partners and other matters that could affect the availability or commercial potential of the Company's product candidates, business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises such as the novel coronavirus (referred to as COVID-19). These risks are not exhaustive, Aptevo faces known and unknown risks. Additional risks and factors that may affect results are set forth in Aptevo's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the fiscal year ended December 31, 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 Aptevo's expectations in any forward-looking statement. Any forward-looking statement speaks only as of the date of this press release, and, except as required by law, Aptevo does not assume any obligation to update any forward-looking statement to reflect new information, events, or circumstances.

Aptevo at-a-Glance



- Clinical-stage immunotherapy company focused on developing novel immuno-oncology therapeutics
- 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
- Clinical portfolio: Lead candidate, APVO436, currently in Phase 1b clinical trials, for the treatment of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)¹
 - Positive results reported for the dose escalation trial (AML/MDS)
 - Results published in two peer-reviewed journals, presented at ASH
 - Activation of expansion trial reported (AML only)²
 - Reported complete remission in combination cohort, patient received transplant
 - Reported significant clinical response in monotherapy cohort, patient received transplant
- Broad preclinical portfolio: Multiple novel candidates in development
 - ALG.APV-527: Designed for treatment of both solid and liquid tumors expressing tumor antigen 5T4; planned IND 2H22
 - APVO603: Designed for treatment of solid tumors
 - APVO442: Designed for treatment of prostate cancer; lower affinity, monovalent anti-CD3 designed to improve biodistribution to prostate tumors

Experienced Leadership



Senior Management

Marvin White – President & CEO Emergent Director; Former CFO, St. Vincent's Health; Former Executive Director & CFO, Lilly USA

Jeff Lamothe – EVP, CFO Former Emergent VP, Finance; Former CFO, Cangene Corporation

Dirk Huebner, MD – Chief Medical Officer*

Former CMO of Mersana, Head of Development of Boston Biomedical, Executive Medical Director of Millennium/Takeda

Jane Gross, Ph.D. – Chief Scientific Officer*

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

SoYoung Kwon – SVP, GC, Corporate Affairs & HR

Former SVP, GC and Corporate Secretary, AGC Biologics

Daphne Taylor- VP, Finance

Former Chief Financial Officer at BioLife Solutions, VP, Chief Accounting Officer & Controller at Cardiac Science Corporation

Board of Directors

John Niederhuber, M.D. Inova Translational Medicine Institute; National Cancer Institute; Johns Hopkins University

Marvin White

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

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

Extensive R&D, Manufacturing, Commercial and Financial Expertise and Experience

*Drs. Huebner and Gross are consultants to the Company.

Robust Pipeline: Potential for Multiple Shots on Goal in Hematologic Malignancies and Solid Tumors



Product/	Technology	Potential Indications	Pre- Clinical	Clinical Development Stage				
Candidate Target				Phase I	Phase II	Phase III	Marketed	Milestones/Highlights
APVO436 CD3/CD123	Redirected T cell Cytotoxicity (RTCC)	AML/MDS						Phase 1 dose escalation reported positive results; Part 2 dose expansion on- going
ALG.APV-527* 4-1BB/5T4	T cell Co-Stimulation	Solid Tumors		I				Advancing into clinical development in solid tumors expressing 5T4. IND planned: 2H22
APVO603 4-1BB/OX40	Dual T cell Co-stimulation	Solid Tumors						Unique asset for use in solid tumors, APVO603 lead candidate identified
APVO442 PSMA/CD3	Redirected T cell Cytotoxicity	Prostate Cancer						Low affinity CD3, advancing lead candidate

APVO436 Phase 1b Expansion Trial



Overview

- Multi-center, multi-cohort trial with all cohorts enrolling simultaneously
- Cohorts include both monotherapy and combination protocols, including current, standard of care therapies
- The Company plans to use the outcomes from the Phase 1b trial to inform the APVO436 advanced clinical program

Status

- The trial is on-going
- Reported complete remission in combination cohort, patient received transplant
- Reported significant clinical response in monotherapy cohort, patient received transplant
- The expansion trial is designed to evaluate the safety and tolerability of APVO436 when it is used as an adjunct to the standard of care and as monotherapy, and to obtain a preliminary assessment of the anti- leukemia activity of APVO436 in both modalities

Corporate Strategy



1

Advance lead candidate, APVO436, via multi-center, five cohort phase 1 expansion trial



Demonstrate the promise of the pipeline by pursuing strategic collaborations and partnerships



Develop and advance novel differentiated immunooncology product candidates using the ADAPTIR and ADAPTIR-FLEX platform technologies



Maximize non-dilutive funding opportunities to support efficient pipeline advancement

Platform Technologies

ADAPTIR – Modular Bispecific Platform Technology Supports Development of Novel Therapeutics



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)
- Stimulation of activating receptors to re-invigorate immune response
- Bispecifics can be developed to block inhibitory receptors to improve anti-tumor responses.

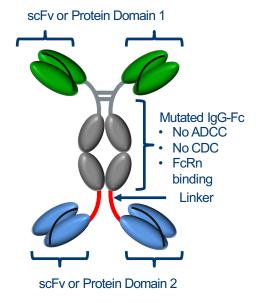
Excellent Manufacturability Characteristics

- Based on IgG1 antibody backbone
- Designed to minimize proteolytic cleavage and posttranslational modifications
- Standard manufacturing process with high yields and purity

Antibody-like Half-Life

Enables weekly dosing in humans

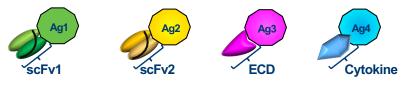
Lead candidate in clinical trials, multiple mechanisms being evaluated



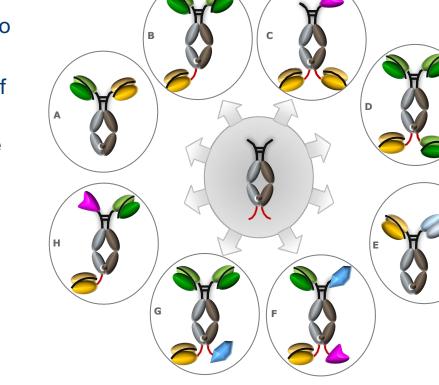
ADAPTIR-FLEX: Heterodimer Platform Technology Overview



- Heterodimer platform technology designed to produce bispecific and multispecific antibody 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 engineer mutations to eliminate
 Fc effector function
- Shares key features with ADAPTIR technology
 - IgG1 backbone and Fc mutations
 - Linkers



Multiple protein domains can be used in design of multi-specific candidates (single chain scFv, extracellular domain ECD, cytokines)

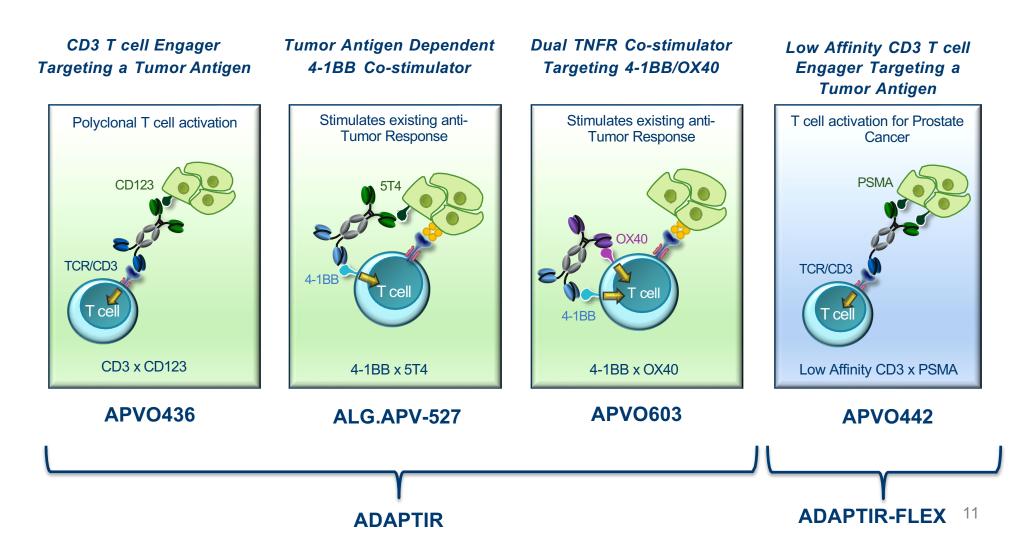


Evolutionary Platform Supports Drug Candidate Diversification

The Pipeline in Action



Platform technologies produce candidates with multiple mechanisms against differentiated targets with the potential to treat both blood and solid tumor cancers



Therapeutic Candidates

APVO436 – Novel Immunotherapy Candidate for AML, Other Leukemias



CANDIDATE	αCD123 scFv αCD3 scFv
OPPORTUNITY	 ADAPTIR (CD123 x CD3) T cell engager Preclinical studies showed reduced cytokines compared to a bispecific T-cell engager from another format*+
TARGET/MOA	 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
POTENTIAL INDICATIONS	 AML, MDS, ALL, hairy cell leukemia, myelodysplastic syndrome Strong unmet need for safe and effective new therapies
DEVELOPMENT STAGE	 Phase 1 study dose escalation in R/R AML and MDS complete Phase 1 study dose expansion in AML active and enrolling Orphan drug designation granted by FDA for AML
PARTNERSHIP STATUS	 Wholly-owned by Aptevo

*Aptevo-generated version of Macrogenics' CD123 x CD3 dual-affinity re-targeting (D.A.R.T) molecule, MGD006 + AACR Annual Meeting, April 2018 AACR on APVO436

The AML / MDS Market*



Strong Unmet Need for Novel Therapies that Improve Outcomes and Survival

- 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.**
 - One in 3 patients with MDS will progress to have AML**
- The global AML market is expected to grow from \$1.4B in 2019 to \$5.1B in 2029 at a compound annual growth rate (CAGR) of 13.6%**
- The U.S. accounts for 65% of total market share and is expected to continue to experience strong growth at a CAGR of 11.9%, through 2029**





Multi-Cer	nter, Multi-Cohort Phase 1 Open-Label Clinical Trial	
Study Design	 Part 1/Dose escalation: Determine maximum tolerated dose and recommended dose for Part 2/Expansion (Completed) Part 2/Expansion: Assess clinical activity at recommended dose (Activated) 	
Administration	Part 1: Intravenous (IV) dosing weekly for 6, 28-day cycles Part 2: IV administration, 4 cycles of therapy, each cycle consists of weekly infusions over a 28-day period	
Subjects	Part 1/Dose escalation: 46 patients Part 2/Expansion: Up to 90 patients	
Status	 Aptevo reported positive data from the dose escalation trial, data published in <i>Cancers</i> and <i>Frontiers in Aging</i>, presented at ASH 2021 Dose expansion trial on-going, to include up to 90 adult patients with AML Reported complete remission in combination cohort, patient received transplant Reported significant clinical response in monotherapy cohort, patient received transplant 	

APVO436 in Phase 1: Dose Escalation Topline Study Results



<u>Overview</u>

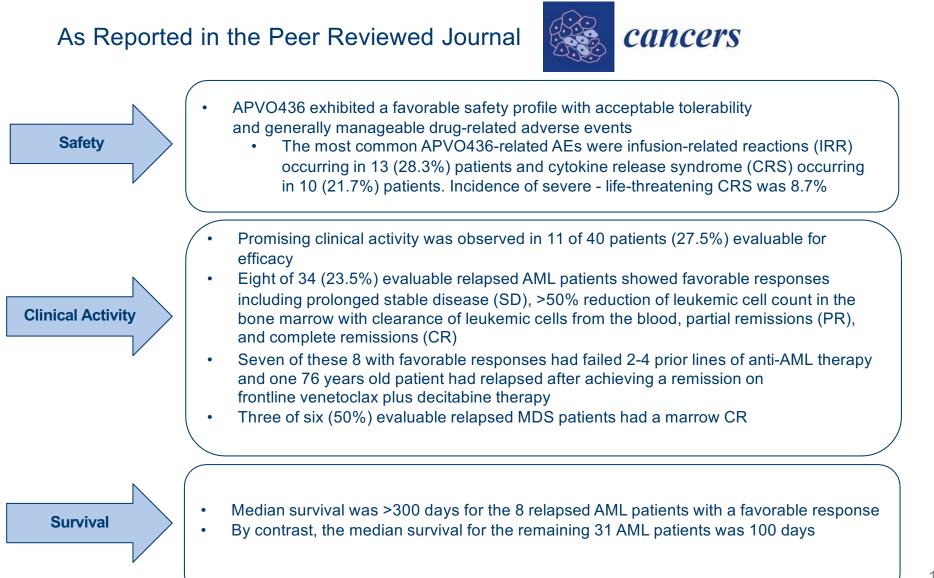
46 patients with AML or MDS

Results

- Primary endpoint achieved: Recommended Phase 2 Dose of 18 mcg identified; maximum tolerated dose not reached at a weekly dose 60 mcg
- APVO436 demonstrated manageable side effects and was well tolerated in the patient population
- Prolonged stable disease, cytolytic responses with clearance of peripheral blasts, partial remissions and complete remissions (CR) observed in AML patients.
- Marrow CRs observed in MDS patients
- Data published in Cancers and Frontiers in Aging, presented at ASH 2021

Phase 1 Dose Escalation Study: A Deeper Dive





APVO436 in Phase 1: Part 2/Expansion



IND Active, Currently Recruiting Patients

<u>Overview</u>

5 cohorts enrolling in parallel at up to 20 trials sites in the U.S. – up to 18 patients per cohort and 90 patients, total.



Relapsed/refractory AML patients: Combination therapy in relapsed patients and those with primary refractory AML that failed to respond to frontline standard induction chemotherapy. Patients will be treated with the standard chemotherapy drug cytarabine or the standard chemotherapy triple drug combination MEC (mitoxantrone, etoposide, cytarabine) plus APVO436.



Poor prognostic but fit primary or secondary AML patients who are treatment-naïve, in first relapse or with primary refractory disease will receive APVO436 in combination with venetoclax and azacytidine.



APVO436 will be administered as monotherapy to AML patients in CR post frontline therapy for consolidation. In addition, patients in first relapse (CR1<1 year) and patients with primary refractory disease will also be enrolled and receive treatment with APVO436.



AML patients in first remission with a MRD+ status following standard of care frontline therapy will receive APVO436 in combination with oral azacytidine.



AML patients in second remission with MRD+ status will receive APVO436 as a dose intensive monotherapy regimen.

Expansion phase trial designed to pursue multiple strategies for APVO436 as a new treatment platform for high-risk and poor prognosis forms of leukemia

Summary: APVO436



- A bispecific T-cell engager candidate designed to target CD123 x CD3
- Half-life of 12.5 days in rodents and 4.5 days in Non-Human Primates
- Preclinical *in vivo* proof-of-concept established in mouse xenograft models of human AML
- CHO cell clone production levels expresses at ~1.5 g/L
- Good manufacturability attributes
- Status of Phase 1b Clinical Trial
 - Dose Escalation: Favorable safety profile, evidence of clinical activity
 - Dose Expansion: Currently enrolling and treating patients

Pipeline Candidates



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

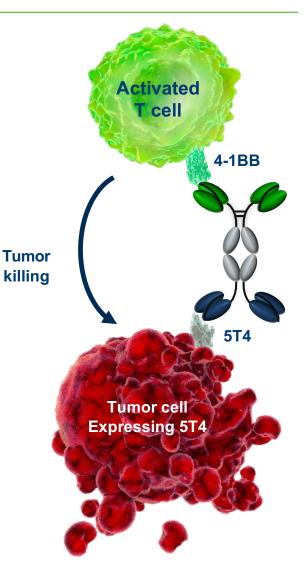


CANDIDATE	α4-1BB scFv α5T4 scFv
OPPORTUNITY	Designed to engage T cells through co-stimulatory receptor 4-1BB
TARGET/MOA	 Targets 4-1BB (co-stimulatory receptor) and 5T4 (tumor antigen) Designed to reactivate antigen-primed T cells to specifically kill tumor cells; designed to promote CD8 T cell survival and effector function
POTENTIAL INDICATIONS	 Multiple solid tumor indications: breast, cervical, non-small- cell-lung, prostate, renal, gastric, colorectal and bladder cancers, with potential in liquid tumors
DEVELOPMENT STAGE	Advancing into clinical development in solid tumors expressing 5T4
PARTNERSHIP STATUS	 Joint 50/50 ownership and co-development agreement with Alligator Bioscience

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



- Designed to simultaneously target
 - 4-1BB is a costimulatory receptor, member of TNFR super family
 - 5T4 is an 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)







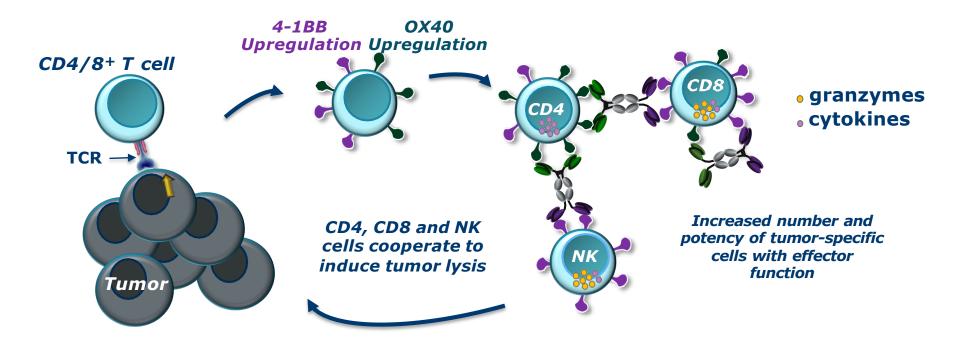
- Designed for 5T4-dependent tumor-directed T-cell activation to overcome dose-limiting toxicities seen with 4-1BB mAbs
- Optimized in the ADAPTIR format for activity, solubility, stability and manufacturability properties
- 5T4-dependent T cell and NK-cell proliferation and activation, 5T4-driven tumor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

APVO603: Dual Agonistic Bispecific Antibody Candidate

CANDIDATE	α4-1BB scFv αΟΧ40 scFv
OPPORTUNITY	 Designed to simultaneously target 4-1BB and OX40 both members of the TNF-receptor family
TARGET/MOA	 Targets two costimulatory receptors 4-1BB and OX40 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
POTENTIAL INDICATIONS	 Solid tumor indications; based on previous anti-tumor T cell response
DEVELOPMENT STAGE	 Preclinical IND-enabling initiated Lead candidate identified; CMC activities in progress
PARTNERSHIP STATUS	Wholly-owned by Aptevo

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 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 POC achieved: Demonstrated 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
- IND-enabling studies underway

APVO442 A Novel Immunotherapy Designed for Prostate Cancer

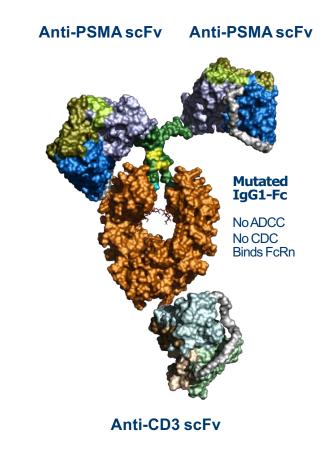


CANDIDATE	Anti-PSMA scFv Mutated IgG1-Fc No ADCC No CDC Binds FcRn Anti-CD3 scFv		
OPPORTUNITY	 αPSMA x αCD3 (low affinity) T cell Engager 		
TARGET/MOA	 Engages T cells via CD3 epsilon to lyse tumor cells expressing PSMA Low-affinity CD3 reduces binding to circulating T cells Designed to enable better biodistribution to solid tumors Low levels of cytokines demonstrated in preclinical studies 		
POTENTIAL INDICATIONS	 Metastatic castration-resistant prostate cancer and other PSMA(+) tumors 		
DEVELOPMENT STAGE	 Lead candidate selected Pre-clinical studies ongoing 		
PARTNERSHIP STATUS	Wholly-owned by Aptevo		

Low Affinity Anti-CD3:

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 CD3engagers against other solid tumors



Summary: APVO442



- 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

The Company





- Effective 03/30/21: Sold RUXIENCE[®] Royalty Stream (Pfizer rituximab biosimilar) to an entity managed by HealthCare Royalty Management, LLC ("HCR") for \$35 million up front, plus additional milestones of up to \$32.5 million
- Upon achievement of HCR aggregate royalty payments totaling 190% of the upfront amount plus milestones paid, Aptevo is also entitled to 50% of any royalty payments made by Pfizer thereafter. 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

* 2021 milestone earned. Payment received in 1Q22

** Based on reported sales in 4Q21, the Company is optimistic that the thresholds for milestones in 2022 and 2023 will be met

Milestones: 2022-2023



Development/Clinical

- Complete APVO436 Phase 1b dose expansion trial (in process)
- Submit an IND for ALG.APV-527 in collaboration with Alligator Bioscience (Planned: 2H22)
 - Evaluate potential in solid tumors expressing 5T4
- APVO603; continue IND-enabling studies
- Advance preclinical development of APVO442
- Explore potential for additional candidate(s) using ADAPTIR and/or ADAPTIR-FLEX platform technologies

Operational/Financial

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

Why Aptevo



Expertise Established leadership position designing protein-based therapeutic candidates for cancer



Technology

Proprietary, versatile, differentiated ADAPTIR and ADAPTIR-FLEX platform technologies that enable generation of new pipeline candidates



Achievement

Advancing pipeline of clinical and preclinical bispecific candidates, APVO436 leading the way



Opportunity

Deep portfolio offers multiple opportunities for collaborations and partnerships



Value

Cash runway through 1Q23 Completion of APVO436 expansion trial enrollment and initiation of ALG.APV-527 clinical program expected inside cash window

Focused, innovative and driven in the fight against cancer



Aptevo Therapeutics

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