

11 October 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. 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," "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.

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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.

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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 trial, for the treatment of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)¹
 - Positive results for the dose escalation phase (AML/MDS)
 - Activation² of expansion trial reported (AML)
- Broad preclinical portfolio: Multiple novel candidates in development
 - ALG.APV-527: Designed for treatment of both solid and liquid tumors expressing tumor antigen 5T4
 - 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 – SVP, CFO

Former Emergent VP, Finance; Former CFO, Cangene Corporation

Fatih Uckun M.D. Ph.D. – Consultant and Chief Clinical Advisor

Former Stohlman Scholar of Leukemia Society of America; Former Professor at USC and UM; Member ASCI

Jane Gross, Ph.D. – Consultant and CSO

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

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

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



Product/ Candidate Target	Technology	Potential Indications	Pre- Clinical	Clinical Development Stage				
				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 active and recruiting
ALG.APV-527* 4-1BB/5T4	T cell Co-Stimulation	Solid Tumors						Advancing into clinical development in solid tumors expressing 5T4
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

Part 2 of APVO436 Phase 1b Study Activated with Five Concurrent Expansion Cohorts



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

COHORT

- 1
- Combination therapy in relapsed patients and those with primary, refractory AML with leukemia that failed to respond to frontline standard induction chemotherapy
- 2
- Combination therapy for AML patients in first relapse and as frontline in newly diagnosed AML patients with poor prognosis
- 3
- •Monotherapy for consolidation after induction chemotherapy in AML patients with poor prognosis and AML patients with early first relapse (within one year of receiving frontline therapy)
- 4
- Combination therapy in AML patients who are in first remission with minimal residual leukemia
- 5
- Monotherapy in AML patients who are in second remission with minimal residual leukemia

Corporate Strategy



- Advance lead candidate, five cohort phase 1 expansion trial
 - APVO436, via multi-center,
- **Develop and advance novel** differentiated immunooncology product candidates using the **ADAPTIR and ADAPTIR-FLEX platform technologies**

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

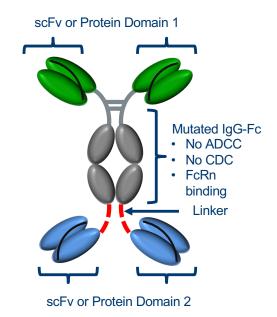
- Redirected T-Cell Cytotoxicity (RTCC)
- Stimulation of activating receptors to re-invigorate immune response
- Bispecifics can be developed to block inhibitory receptors to improve anti-tumor responses.

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



9

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

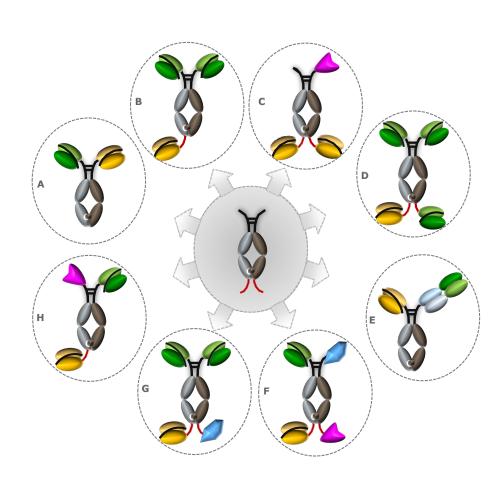








Multiple protein domains can be used in design of multi-specific candidates (single chain scFv, extracellular domain ECD, cytokines)



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

CD3 T cell Engager Targeting a Tumor Antigen

Polyclonal T cell activation

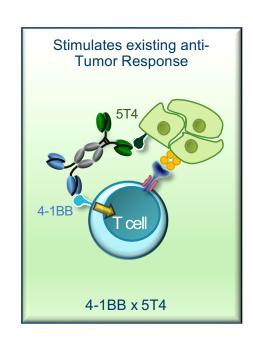
CD123

TCR/CD3

CD3 x CD123

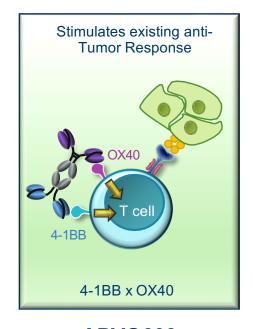
APVO436

Tumor Antigen Dependent 4-1BB Co-stimulator



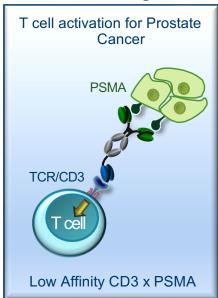
ALG.APV-527

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



APVO603

Low Affinity CD3 T cell Engager Targeting a Tumor Antigen



APVO442

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**



^{*}American Cancer Society, Seer.cancer.gov

¹⁴







Multi-Center, 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 (Complete) 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: 90 patients	
Status	Aptevo reported positive data from the dose escalation trial, data published in <i>Cancers</i> Aptevo reported that the expansion part of the trial was active and recruiting and will include five concurrent cohorts of 18 patients each	

APVO436 in Phase 1: Dose Escalation Topline Study Results



Overview

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

APVO436 in Phase 1 Dose Escalation Study: A Deeper Dive



Published in the Peer Reviewed Journal



In the paper we reported:

Safety

- APVO436 exhibited a favorable safety profile with acceptable tolerability and generally manageable drug-related adverse events
 - The most common APVO436-related AEs were infusion-related reactions (IRR) occurring in 13 (28.3%) patients and cytokine release syndrome (CRS) occurring in 10 (21.7%) patients. Incidence of severe life-threatening CRS was 8.7%

Clinical Activity

- Promising clinical activity was observed in 11 of 40 patients (27.5%) evaluable for efficacy
- Eight of 34 (23.5%) evaluable relapsed AML patients showed favorable responses including prolonged stable disease (SD), >50% reduction of leukemic cell count in the bone marrow with clearance of leukemic cells from the blood, partial remissions (PR), and complete remissions (CR)

APVO436 in Phase 1Dose Escalation Study: A Deeper Dive



Reported in the Peer Reviewed Journal



Clinical Activity (continued)

- Seven of these 8 with favorable responses had failed 2-4 prior lines of anti-AML therapy and one 76 years old patient had relapsed after achieving a remission on frontline venetoclax plus decitabine therapy
- Three of six (50%) evaluable relapsed MDS patients had a marrow CR

Survival

- Median survival was >300 days for the 8 relapsed AML patients with a favorable response
- By contrast, the median survival for the remaining 31 AML patients was 100 days

APVO436 in Phase 1: Part 2/Expansion



IND Active, Currently Recruiting Patients

Overview

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

Cohort

- 1
- **Relapsed AML patients:** Combination therapy in relapsed patients and those with primary, refractory AML with leukemia 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
- 2
- **AML patients in first relapse** will receive a combination of APVO436 + venetoclax + azacitidine. Also included in this cohort will be newly diagnosed AML patients with a poor prognosis who will receive this novel combination as their frontline induction regimen
- 3
- AML patients with poor prognosis and with early first relapse (within one year of receiving frontline therapy) will receive frontline chemotherapy to induce a remission and APVO436 will be added if there is evidence of residual leukemia
- 4
- Combination therapy in AML patients who are in first remission with minimal residual leukemia, will receive the standard drug oral azacytidine in combination with APVO436

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 part: Favorable safety profile; the recommended Phase 2 dose level (RP2D) identified
 - Dose Expansion part: At designed recommended Phase 2 dose (RP2D) and IRBapproved with 5 independent, parallel cohorts

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

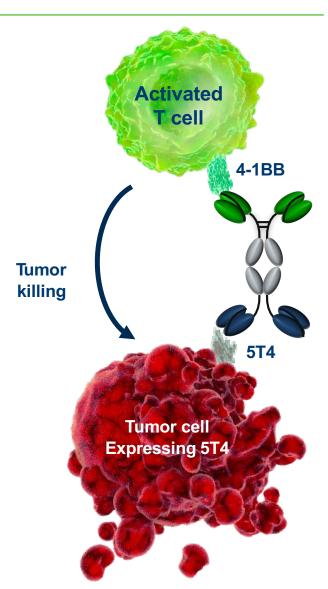


CANDIDATE	α4-1BB scFv α5T4 scFv
OPPORTUNITY	Designed to engage T cells through co-stimulatory receptor 4-1BB
TARGET/MOA	 Targets 4-1BB (co-stimulatory receptor) and 5T4 (tumor antigen) Designed to reactivate antigen-primed T cells to specifically kill tumor cells; designed to promote CD8 T cell survival 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)



Summary: ALG.APV-527



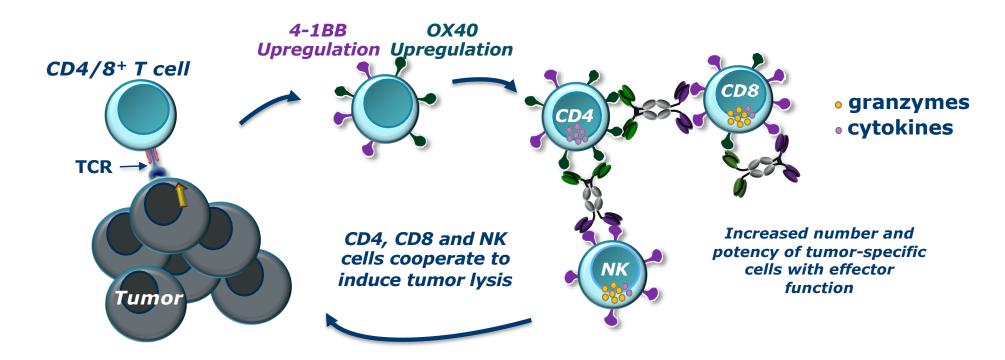
- Designed for 5T4-dependent tumor-directed T-cell activation to overcome dose-limiting toxicities seen with 4-1BB mAbs
- Optimized in the ADAPTIR format for activity, solubility, stability and manufacturability properties
- 5T4-dependent T cell and NK-cell proliferation and activation, 5T4-driven tumor 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 αOX40 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 and CMC activities initiated 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

Summary: APVO603



- 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

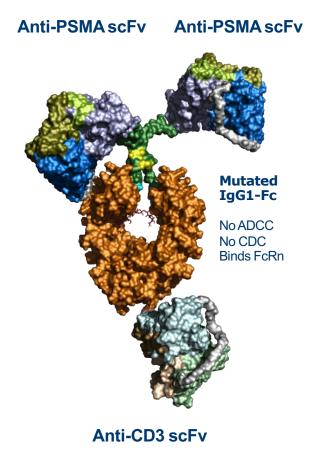


CANDIDATE	Anti-PSMA scFv Mutated IgG1-Fc No ADCC No CDC Binds FcRn Anti-CD3 scFv		
OPPORTUNITY	αPSMA x αCD3 (low affinity) T cell Engager		
TARGET/MOA	 Engages T cells via CD3 epsilon to lyse tumor cells expressing PSMA Low-affinity CD3 reduces binding to circulating T cells Designed to enable better 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: Designed to Improve Solid Tumor Biodistribution Aptevolution

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

 If earned, collection of the above milestones will provide further non-dilutive funding to the Company

Anticipated Milestones: 2021-2022



Development/Clinical

- Initiate and complete APVO436 Phase 1b dose expansion trial (five cohorts of 18 patients per cohort)
- Present Phase 1 dose escalation data at a major oncology conference
- Advance ALG.APV-527 into clinical development in collaboration with Alligator Bioscience
 - Evaluate potential in solid tumors expressing 5T4
- APVO603; initiate 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



- 1
- **Expertise**

Established leadership position designing protein-based therapeutic candidates for cancer

2

Technology

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

3

Achievement

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

4

Opportunity

Deep portfolio offers multiple opportunities for collaborations and partnerships

5

Value

Cash runway through Q3 2022 APVO436 expansion trial data expected inside cash window



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