Aptevo Therapeutics

Bispecifics Differentiated by Design

March 27, 2024 | Nasdaq: APVO

Forward-Looking Statements

March 2024 | Nasdaq: APVO

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, statements related to the progress of Aptevo's clinical programs, including statements related to anticipated clinical and regulatory milestones such as a Phase 1b/2 trial initiation for APVO436, whether the Phase 1b/2 protocol will be successful, whether further study of APVO436 in Phase 1b/2 trial focusing on a targeted patient population will continue to show clinical benefit, whether Aptevo's strategy will translate into an improved overall survival in AML, statements related to the durability of APVO436 and whether its duration of remission results will be indicative of later stage clinical trials, whether the APVO436 data in combination therapy and monotherapy will be indicative of later stage clinical trials, APVO436's potential for multiple indications, and the timing for its expected data readouts, ALG.APV-527's potential for multiple indications, and the timing for its expected preliminary data, the possibility of meaningful data readouts for ALG.APV-527, whether the diversified pipeline candidates will demonstrate the ability to fight a range of solid malignancies, expectations regarding the effectiveness of its ADAPTIR and ADAPTIR-FLEX platforms, whether Aptevo will continue to have momentum in its business in the future, statements related to Aptevo's cash position and balance sheet, statements related to Aptevo's ability to generate stockholder value, and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "optimism," "potential," "designed," "engineered," "innovative," "innovation," "promising," "plans," "forecasts," "estimates," "will" and similar expressions. Investors are, therefore, cautioned not to place undue reliance on any forward-looking statement. 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.

There are several important factors that could cause Aptevo's actual results to differ materially from those indicated by such forward-looking statements, including a deterioration in Aptevo's business or prospects; further assessment of preliminary data or different results from later clinical trials, adverse events and unanticipated problems, adverse developments in clinical development, including unexpected safety issues observed during a clinical trial; the market potential of Aptevo's therapeutic candidates; and changes in regulatory, social, macroeconomics 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 results of preliminary data and pre-clinical studies being predictive of the results of later-stage clinical trials, initiation, enrollment and maintenance of patients, and completion of clinical trials, availability and timing of data from ongoing clinical trials, the trial design includes combination therapies that may make it difficult to accurately ascertain the benefits of a product candidate, expectations for the timing and steps required in the regulatory review process, expectations for regulatory approvals, the impact of competitive products, our ability to enter into agreements with strategic partners or raise funds on acceptable terms or at all, and other matters that could affect the availability or commercial potential of the Company's product candidates or business, economic disruptions due to catastrophes or other events, including natural disasters or public health crises such as the coronavirus (referred to as COVID- 19), and geopolitical risks, including the current war between Russian and Ukraine and macroeconomic conditions such as economic uncertainty, rising inflation and interest rates, conditions in the banking system and financial markets, including the failure of banks and financial institutions, increased market volatility and decreased consumer confidence. 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, 2023, and its subsequent quarterly 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 presentation, 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.

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Bispecifics Differentiated by Design

Investment Highlights

Large Market Opportunity	• Targeting both solid tumors and hematologic cancers • Multi billion-dollar opportunities • Significant unmet needs = opportunities for new entrants in many markets
Differentiated Assets	• Unique and favorable safety profile • Precision targeted vs. systemic exposure • Combinable with other MOA's
Derisked Clinical Path/Promising Early Clinical Data	• 90 patients dosed in AML trials – drug is safe and tolerable • Promising efficacy data in AML – better than benchmarks • Promising early data in solid tumor trial
Near Term Inflection Points	• Multiple data readouts over next 12 months in both clinical programs • Next phase trial initiations planned for both programs
Experienced Management	• Experienced team with broad and diverse healthcare industry backgrounds • Expertise spans drug discovery to commercialization

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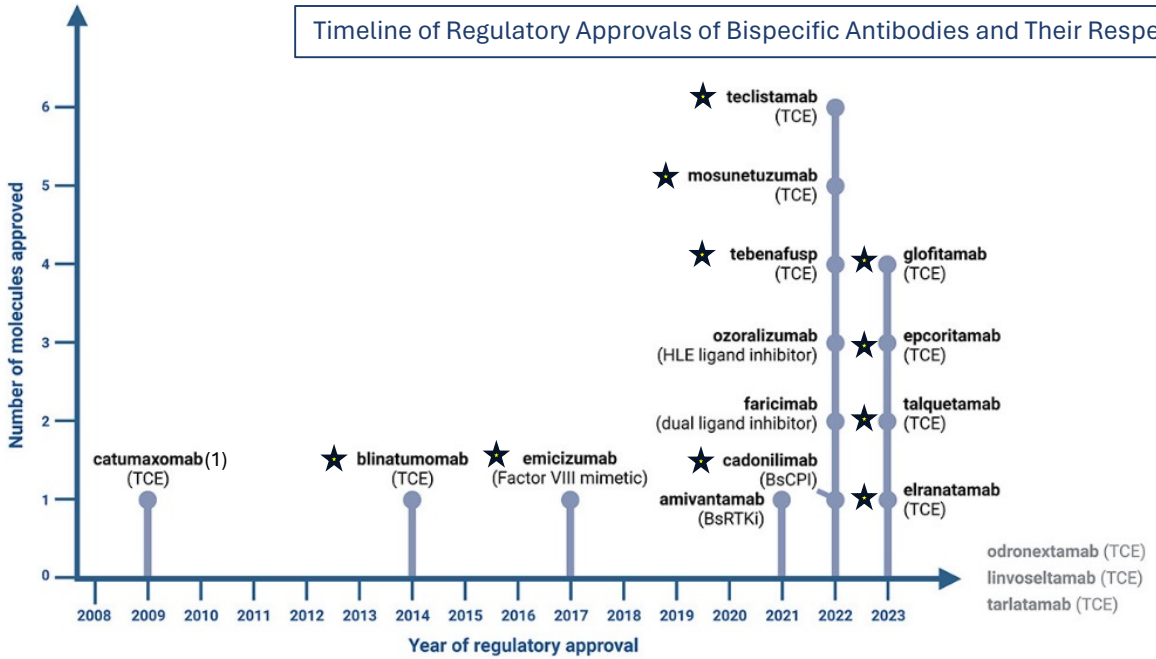
Bispecifics Are Having Their Day

- ✓ **11 of the 13** approved bispecifics have received approval since 2021, including some accelerated approvals
- ✓ 80% of active bispecific clinical trials have entered the clinic **within the last 5 years**
- ✓ Bispecifics are in development in **both hematologic malignancies and solid tumors**

Timeline of Regulatory Approvals of Bispecific Antibodies and Their Respective Mechanisms of Action



Of the 13 currently approved bsAbs (bispecific antibodies), two…have achieved blockbuster status, showing the promise of this novel class of therapeutics. In the 2020s, the approval of additional bsAbs can be expected in hematological malignancies, solid tumors and non-oncology indications, establishing bsAbs as essential part of the therapeutic armamentarium. [2]

★ Oncology related
(1) No longer commercially marketed
Source: A Pivotal Decade for Bispecific Antibodies? March 11, 2024
TCE = T Cell Engager
[2] A Pivotal Decade for Bispecific Antibodies?

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Aptevo's Differentiated & Diversified Bispecifics

Built to Overcome Common Safety Challenges

- ✓ Unique CD3 designed to **reduce cytokine release syndrome** (CRS) as seen in APVO436 clinical results
- ✓ Stimulatory binding domains only function when crosslinked, **eliminating systemic off target immune activation**, potentially reducing or eliminating toxicities

Enhance Tumor-Specific Functions

- ✓ Binding domains used are known to be expressed on tumor or within the tumor microenvironment that **localize the bispecific to tumors**
- ✓ Reduced affinity CD3 with potential to increase tumor localization (APVO442)
- ✓ Checkpoint inhibitor to block the PD-1/PD-L1 pathways (APVO711)
- ✓ **Costimulation** via 4-1BB, OX40 or CD40 augment the antitumor response (APVO603, ALG.APV-527, APVO711)

- ✓ **Combinable with standard of care** or other experimental therapies (i.e. radiopharmaceuticals, antibody drug conjugates (ADC's), adaptive T cells, checkpoint molecules, other bispecifics)
- ✓ CHO production cell lines used with antibody-like purification

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Diversified Pipeline Offers Multiple Opportunities for Partnering

	Program (Target)	Potential Indication(s)	Preclinical	Phase 1 (First-in-Human)	Phase 2	Notes
Clinical Programs	**APVO436** (CD3 x CD123)	Frontline AML	→	→		**Orphan Drug Designation** APVO436 in combination with venetoclax and azacitidine
Clinical Programs	**ALG.APV-527*** (4-1BB x 5T4)	NSCLC, Head & Neck, Colorectal, Pancreatic, Breast, Other Solid Tumors	→	→		Phase 1 trial ongoing, interim results 2Q24
Pre-Clinical Programs	**APVO711** (PD-L1 x CD40)	Multiple solid tumors	→			Preclinical studies ongoing
Pre-Clinical Programs	**APVO603** (4-1BB x OX40)	Multiple solid tumors	→			IND enabling studies ongoing
Pre-Clinical Programs	**APVO442** (PSMA x CD3)	Prostate Cancer	→			IND enabling studies ongoing

*Partnered with Alligator Bioscience

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Clinical Candidates Targeting Large Markets

Aptevo molecules capable of targeting multiple cancers with large market potential

Select Global Market Opportunities*	Size
AML	$2.5B
MDS	$1.8B
Breast Cancer	$32.1B
Non-Small Cell Lung Cancer	$24.2B
Colorectal Cancer	$15.8B
Head and Neck Cancer	$2.8B
Pancreatic Cancer	$2.7B
Cervical Cancer	$2.2B

* Source: Global Data

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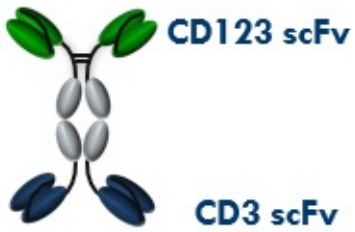
APVO436
AML, MDS and Other Leukemias

"The APVO436 results are promising and show that APVO436 is well-suited to combine with the venetoclax + azacitidine standard of care regimen. We see a very manageable safety profile and promising efficacy, including duration of remission results."

Justin Watts, MD, Associate Professor of Medicine,
Division of Hematology, Chief, Leukemia Section,
University of Miami/Sylvester Comprehensive Cancer Center

Novel Bispecific Drug for AML and Other Leukemias



POTENTIAL INDICATIONS

Multiple blood cancers, including AML and MDS

Combinable with standard of care (venetoclax & azacitidine) with demonstrated improved patient outcomes

UNIQUE DESIGN

- Designed to engage T cells via CD3 binding to specifically kill CD123-expressing tumor cells. CD123 is a compelling target for AML due to its overexpression on leukemic stem cells and AML blasts
- Our CD3 binding domain is derived from CRIS-7; unique from competitors. Preclinical studies compared to a competitor candidate demonstrated reduced cytokine secretion which has translated into manageable CRS in the clinic
- Combination of potent microgram dose level and typical CHO manufacturing yield translates into extremely low cost per dose
- Convenient weekly I.V. dosing in the clinic vs. some competitors delivering by continuous infusion

OWNERSHIP

- Wholly-owned by Aptevo Therapeutics
- Core family patent exclusivity until 2037
- Orphan drug designation granted by FDA for AML

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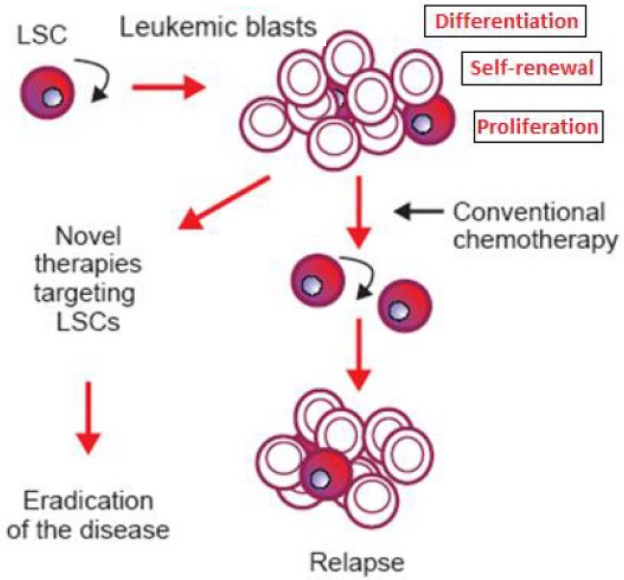
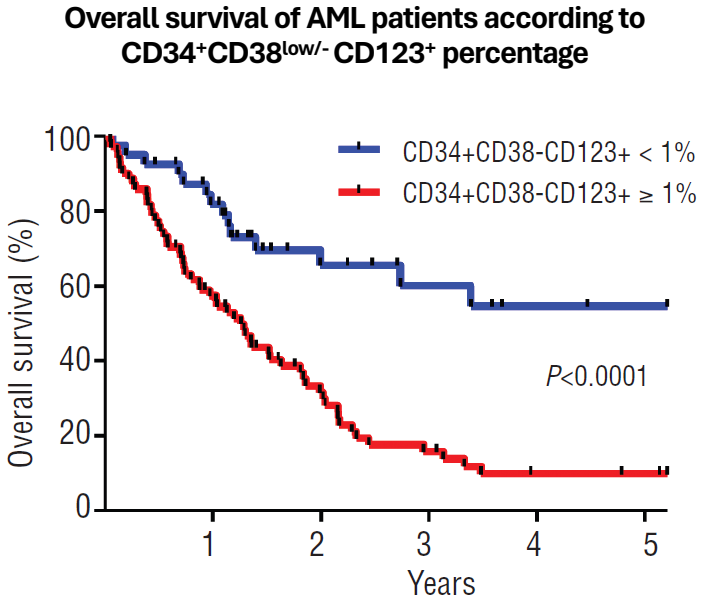
Why We are Targeting CD123

- CD123 (an IL3 receptor which creates an anchor for our unique CD3) is an antigen that is **overexpressed** in AML and MDS cells which makes this a meaningful therapeutic target
- CD123 is also expressed on **leukemic stem cells (LSC's),** which are self-renewing, making them resistant to chemotherapy, thus killing of these cells with our CD3 T cell engager (TCE) **reduces potential for relapse**
- Clinical data demonstrates that the presence of LSC's is associated with poor overall survival – **reducing the amount of LSC's can prolong patient survival**
- No other bispecifics approved or in late-stage development targeting CD123





https://pubmed.ncbi.nlm.nih.gov/21933861/,
https://journals.sagepub.com/doi/epdf/10.1177/107327480401100216

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APVO436: Clinical Progress
Entering Frontline Dose Optimization Phase in 2Q 2024

Trial Design

Dose Escalation (Monotherapy)

- 46 patients treated with monotherapy at escalating dose levels to assess safety (AML & MDS)

Dose Expansion (Combination + monotherapy)

- 44 AML patients treated in both monotherapy and in various combinations to assess safety and efficacy
- Broad population including frontline and relapsed/refractory patients

Dose Optimization 1H2024 (Part 1 of Phase 1b/2) (Combination)

- This phase patient population: Frontline AML patients who are not eligible for intensive induction due to age or other factors
- Up to 39 patients in escalating dose level cohorts to further explore efficacy and safety in combination with the standard of care venetoclax + azacitidine

Compelling Results to Date

Dose Escalation

- 2 complete responses (CR's) reported in AML patients who received the drug as a monotherapy
- Most CRS cases were low-grade and clinically manageable

Dose Expansion

- **91% clinical benefit rate** in combination with standard of care venetoclax + azacitidine in venetoclax naïve patients which exceeds our benchmark*
- **Clinically meaningful duration of remission**, with no median reached – multiple patients either stayed on treatment or moved to transplant
- **27% of patients experienced CRS** (cytokine release syndrome), which is favorable compared to competitor drugs.
- Most CRS cases were low-grade and clinically manageable

Upcoming Milestones

- Expected to commence in 2Q2024
- Interim data readouts (open label) expected during 2H2024 & 1H2025
- Part 1b dose optimization trial complete, preliminary data anticipated 1H2026

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*Benchmark Composite References: Aldoss 2019, Maiti 2021, Morsia 2020, Garciaz 2022, Feld 2021

APVO436 CRS Data Tells a Positive Story

Incidence of CRS

	Dose Escalation	Dose Expansion	Total	
# Patients	**46**	**44**	**90**	
	#	**#**	**#**	**%**
All CRS	12	12	24	27
CRS Grade ≥ 3	4	2	6	7

The Takeaways

- Of the 90 patients treated with APVO436, only 27% experienced CRS
- 7% of patients had CRS cases grade 3 or higher
- Side effects were generally manageable in the clinic

CRS = Cytokine release syndrome

Efficacy Outperforms Benchmarks

Data from the dose expansion supports continued development of APVO436 in frontline patients in combination with standard of care venetoclax + azacitidine

Patients Receiving Combination of Venetoclax + Azacitidine + APVO436

Response Type	Patient Type	
	All	Ven-naïve
# Patients enrolled	19	12
# Patients evaluable	16	11
CR, n	5	5
CRi, n	3	3
MLFS, n	1	1
SD, n	3	1
Clinical Benefit Rate %	**75%**	**91%**
Composite CR %	**56%**	**82%**
CR/CRi %	**50%**	**73%**
CR %	**31%**	**45%**

CR: Complete remission, CRi: Complete remission with incomplete hematologic recovery, MLFS: Bone marrow complete remission, SD; Stable disease, CBR: (Clinical benefit rate) consists of CR, CRi, MLFS and SD, Composite CR: Consists of CR, CRi and MLFS

The Takeaways

- 91% clinical benefit rate in patients receiving combination treatment (venetoclax + azacitidine + APVO436) in venetoclax treatment naïve patients
- This combination outperforms the benchmarks as follows:

	APVO436	Benchmark*
Composite CR	**82%**	**33-57%**
CR/CRi	**73%**	**21-46%**
CR	**45%**	**13-26%**

*Benchmark Composite References: Aldoss 2019, Maiti 2021, Morsia 2020, Garciaz 2022, Feld 2021.

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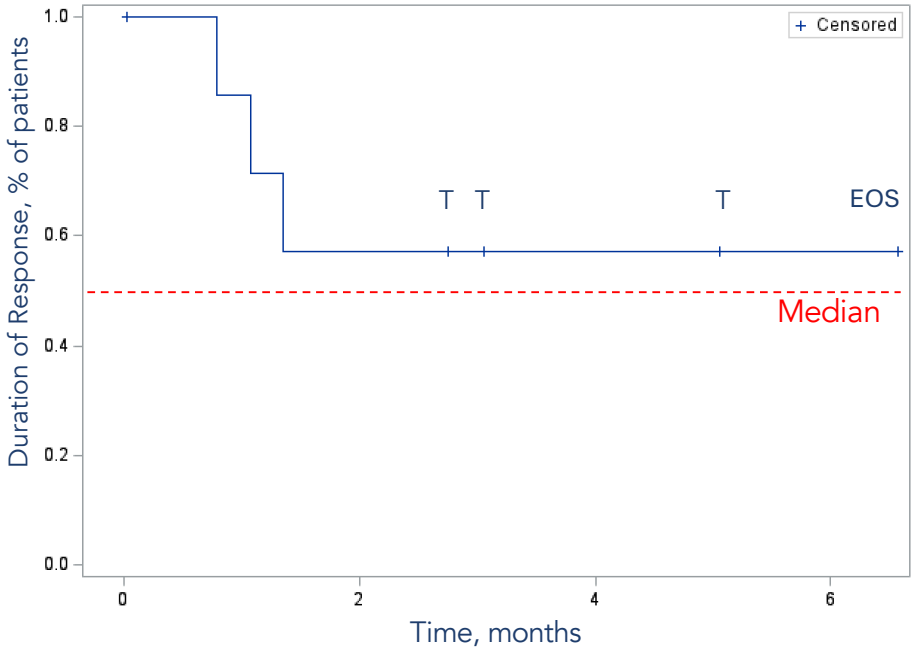
Encouraging Duration of Remission (DOR)

DOR data adds to a growing body of clinical evidence (safety, tolerability, efficacy and duration of remission) and provides strong support for the further development of APVO436 in combination therapy for patients with AML.

- **Multiple patients moved to transplant -** 3/11 patients responded sufficiently to move to stem cell transplant – receiving stem cell transplant is the treatment option with the ***best probability for survival and highest benefit to patients***
- **Sustained complete remission -** Of the patients with responses, one patient remained on study with sustained complete remission for 8 cycles (maximum allowed per protocol)
- **Median DOR not reached -** The median DOR was not reached, which is clinically meaningful because ***a substantial number of patients*** **either stayed on treatment or moved to transplant** and did not experience a relapse event



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ALG.APV-527
Multiple Solid Tumor Type Expressing 5T4

ALG.APV-527: Novel Bispecific Drug for Multiple Solid Tumors

POTENTIAL INDICATIONS

Multiple solid tumor cancers, including lung, breast, head & neck, colorectal, pancreatic, and other solid tumors with significant markets

Unique Design

- Unique mechanism of action allows for targeting of both 4-1BB (co-stimulatory receptor) and 5T4 (tumor antigen)
- Designed to overcome safety issues of others' first-generation 4-1BB agonists by designing ALG.AVP-527 to require 5T4-dependent immune activation
- Promotes the activity of antigen-primed CD8 T cells by increasing survival and enhancing their ability to kill tumor

Ownership

- Joint 50/50 ownership and co-development agreement with Alligator Bioscience
- Patent exclusivity until 2038 (+ up to 5 years patent term extension)

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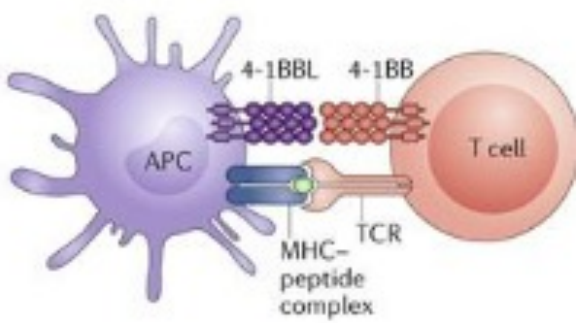
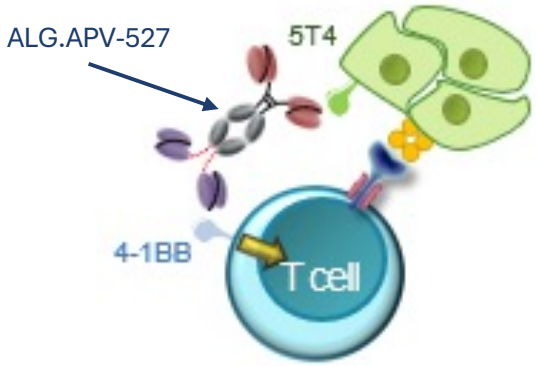
Why We Are Targeting 4-1BB + 5T4

- 4-1BB provides attributes to T cells and NK cells that **enhance tumor cell killing**
- 4-1BB is one of many costimulatory receptors expressed on tumor infiltrating T cells and NK cells but **not on peripheral blood cells**, allows for precision targeting of tumor cells
- 5T4 is an antigen expressed on the tumor indication but NOT highly expressed on normal tissue, further allowing for **precision targeting** and reducing systemic response
- Both 4-1BB and 5T4 are pre-clinically and clinically **validated**

4-1BB Co-Stimulation



4-1BB Co-Stimulation with 5T4 Tumor Antigen Dependency



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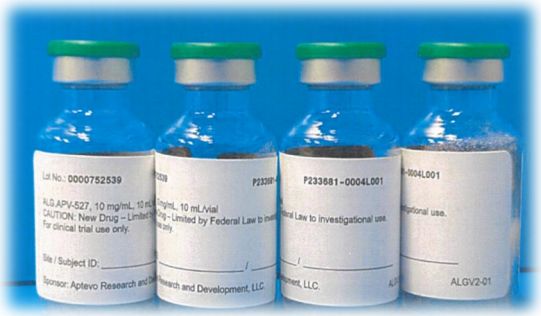
ALG-APV.527 Clinical Progress
Enrollment More than 50% Complete

Trial Design

Objective
- Determine approach for dose expansion population and dose

Dose Escalation
- Multi-center, multi-cohort Phase 1 open-label dose escalation
- Up to 25 patients at escalating monotherapy doses in 3 + 3 trial design
- Multiple solid tumor targets, including lung, breast, head & neck, colorectal, pancreatic

Endpoints
- Assess safety and tolerability, pharmacokinetic, pharmacodynamic and preliminary anti-tumor activity of ALG.APV-527
- Biomarker analysis to confirm pharmacodynamic activity as it relates to efficacy and safety; proof of concept in combination therapy



Compelling Results to Date

Dose Escalation
- ALG.APV-527 could be **measured in all patients** with plasma concentration of ALG.APV-527 consistent with the administered dose
- Biomarker analyses indicate the expression of the targets (4-1BB and 5T4) in tumor biopsies and **confirm biological activity** of ALG.APV-527
- Signs of **clinical activity** were observed for both enrolled patients with heavily **pre-treated breast cancer**

Status
- Enrollment more than 50% complete
- Early trial data reported 1Q24

Milestones
- Enrollment expected to be complete 3Q2024
- Full data readout expected 4Q2024
- Expansion trial initiation expected 1H2025

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ALG.APV-527: Promising Interim Data in Solid Tumors

Early promising data from the ALG.APV-527 multi-center Phase 1 dose escalation trial, that is now more than 50% enrolled, have been reported as follows:

- Treatment was overall well-tolerated, and a maximum tolerated dose has not yet been determined, dose-escalation in higher-dose cohorts is ongoing
- ALG.APV-527 could be measured in all patients with plasma concentration of ALG.APV-527 consistent with the administered dose
- Biomarker analyses indicate the expression of the targets (4-1BB and 5T4) in tumor biopsies and **confirm biological activity** of ALG.APV-527
- **Signs of clinical activity were observed for both enrolled patients with heavily pre-treated breast cancer.**
  - Both patients demonstrated a measurable level of drug in circulation (pharmacokinetic) and reproducible elevation of serum pharmacodynamic markers with dosing, suggesting the drug is biologically active
  - One patient remained on study for seven months
  - A second remains on study beyond nine months. Both patients achieved best overall response of stable disease

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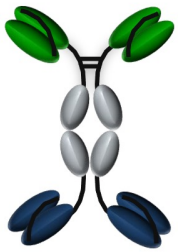
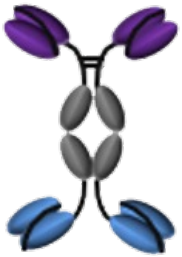
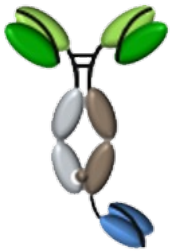
Preclinical Candidates & Platforms

Novel, Solid Tumor-Targeted, Built for Safety

	APV0711	APVO603	APVO442
Diagram	 PD-L1 scFv CD40 scFv	 4-1BB scFv OX40 scFv	 PSMA scFv CD3 scFv
Mechanism of Action	Dual mechanism of action designed to provide synergistic co-stimulation of CD40 on antigen presenting cells and simultaneously block the PD-1/PD-L1 inhibitory pathway	Simultaneously engages two co-stimulatory molecules (4-1BB and OX40) amplifies T cells' effector function	Engages CD3 on T cells which then directly kill PSMA-expressing prostate tumor cells
Unique Design	A checkpoint inhibitor with added functionality CD40 only functions when both binding domains are engaged	Stimulates pre-activated T cells locally in the tumor Only functions when both binding domains are engaged	Low-affinity monospecific CD3 reduces binding to circulating T cells which enables distribution to solid tumors CD3 induces lower levels of cytokines

All potentially combinable with other technologies such as ADC's or radiopharmaceuticals

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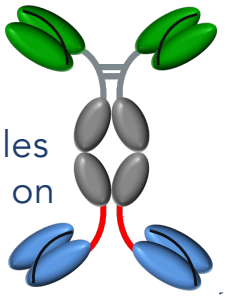
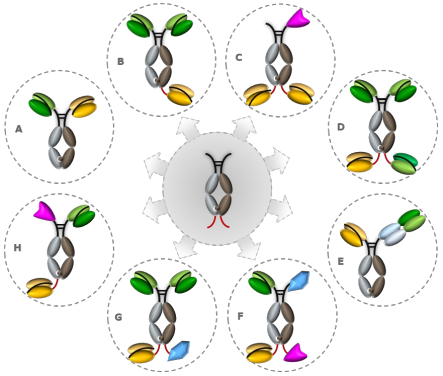
Wholly-Owned Proprietary Platforms

	ADAPTIR	ADAPTIR-FLEX
Drug Targeting	Bind up to two targets 	Binds up to four targets 
Genetic and Structural Format	Single gene that assembles into a homodimer based on an antibody backbone	Two genes that assemble into a heterodimer with a knob-in-hole antibody backbone
	Contains Immunoglobulin Gamma 1 Fc	Contains Immunoglobulin Gamma 1 Fc
Half-life	Demonstrated antibody-like half-life in mice	Demonstrated antibody-like half-life in mice
Effector Function	Fc mutations may be utilized to eliminate binding to Fc Gamma Receptors or to enhance effector function	Fc mutations may be utilized to eliminate binding to Fc Gamma Receptors or to enhance effector function
Manufacturing	Antibody-like manufacturing processes	Antibody-like manufacturing processes
Current Pipeline Candidates	APVO436 (CD123 x CD3) ALG.APV-527 (4-1BB x 5T4) APVO603 (41BB x OX40) APVO711 (PD-L1 x CD40)	APVO442 (PSMA x CD3)

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Additional Information

Experienced & Expert Leadership

Extensive R&D, manufacturing, clinical and financial background

Senior Management

Marvin White, President & CEO

Jeff Lamothe, Chief Operating Officer

Daphne Taylor, Chief Financial Officer

SoYoung Kwon, General Counsel, Business Development & Corporate Affairs

Dirk Huebner, MD, Chief Medical Officer

Board of Directors

John Niederhuber, MD, Chairman

Zsolt Harsanyi, Ph.D., Director

Barbara Lopez Kunz, Director

Daniel Abdun-Nabi, Director

Grady Grant, III, Director

Marvin White, Director

Lilly · St. Vincent Health · EMERGENT · CANGENE · Biolife Solutions · CARDIAC science

ZYMOGENETICS A Bristol-Myers Squibb Company · Takeda · Mersana THERAPEUTICS · BOSTON BIOMEDICAL · AGC Biologics · DIA

INOVA · NATIONAL CANCER INSTITUTE · JOHNS HOPKINS UNIVERSITY · Bristol Myers Squibb · SANOFI GENZYME · BATTELLE It can be done

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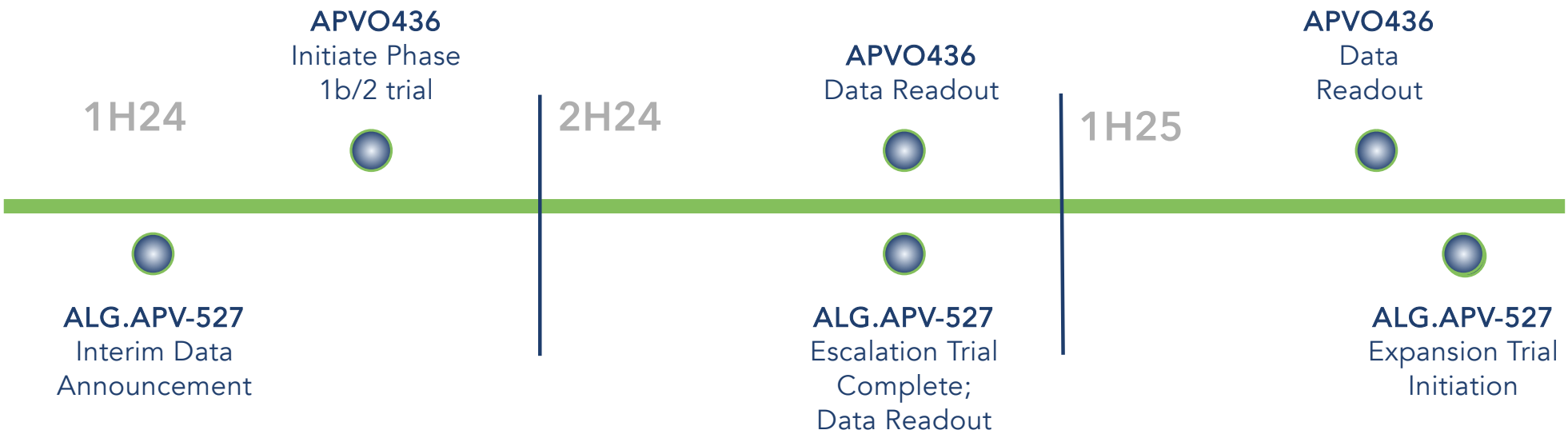
Anticipated Milestones Through Mid-2025



Multiple value-creating opportunities with two clinical drugs in development

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Investment Highlights

Large Market Opportunity	• Targeting both solid tumors and hematologic cancers • Multi billion-dollar opportunities • Significant unmet needs = opportunities for new entrants in many markets
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Derisked Clinical Path/Promising Early Clinical Data	• 90 patients dosed in AML trials – drug is safe and tolerable • Promising efficacy data in AML – better than benchmarks • Promising early data in solid tumor trial
Near Term Inflection Points	• Multiple data readouts over next 12 months in both clinical programs • Next phase trial initiations planned for both programs
Experienced Management	• Experienced team with broad and diverse healthcare industry backgrounds • Expertise spans drug discovery to commercialization

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Thank You

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