



13, August 2024 | Nasdaq: APVO

# Forward-Looking Statements

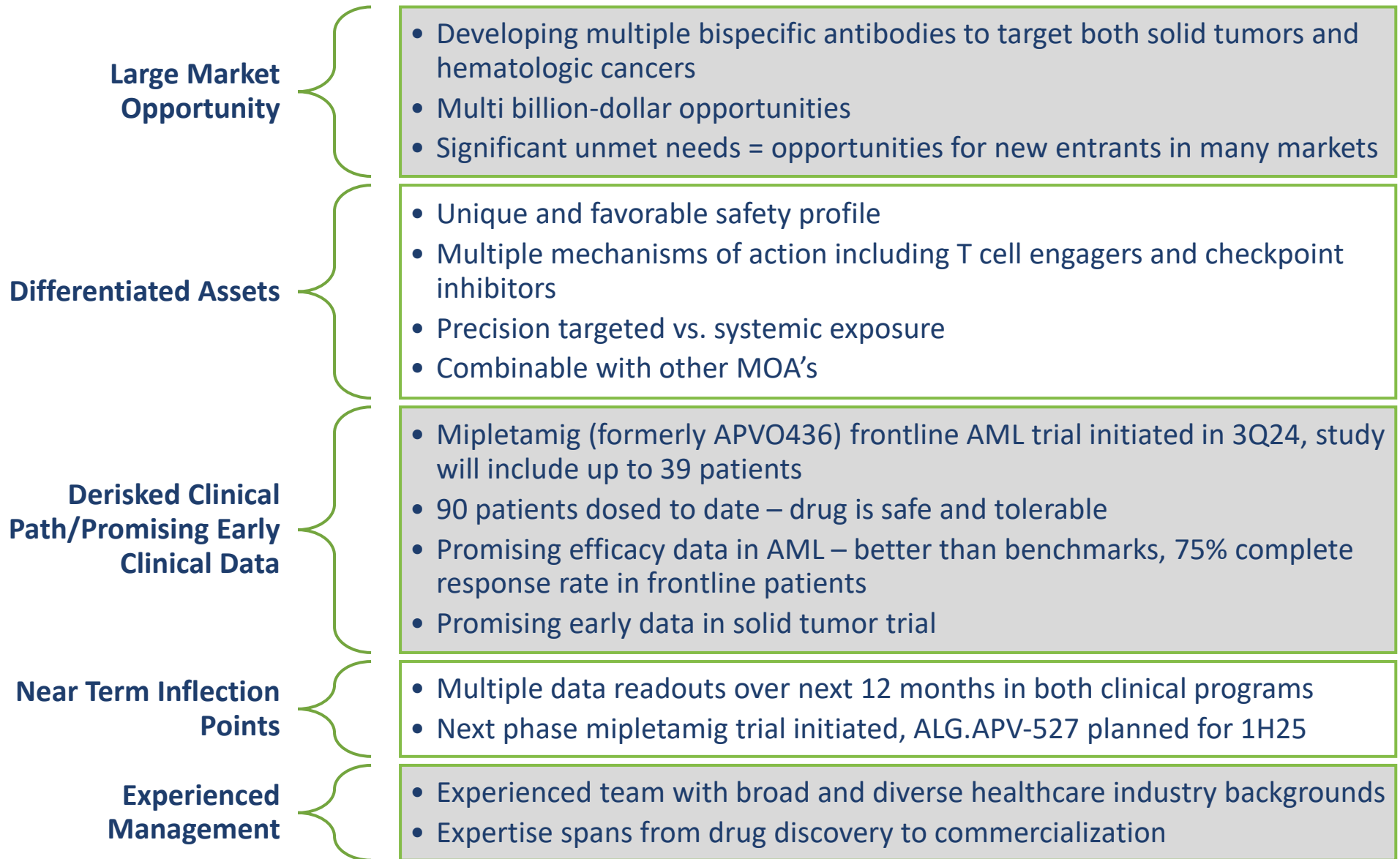
June 2024 | Nasdaq: APVO

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 the Phase 1b/2 trial initiation for mipletamig, whether the Phase 1b/2 protocol will be successful, whether further study of mipletamig 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 rate in acute myeloid leukemia (AML), statements related to the durability of mipletamig and whether its duration of remission results will be indicative of later stage clinical trials, whether the mipletamig data in combination therapy and monotherapy will be indicative of later stage clinical trials, mipletamig'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 as well as the war between Israel and Hamas 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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# Investment Highlights



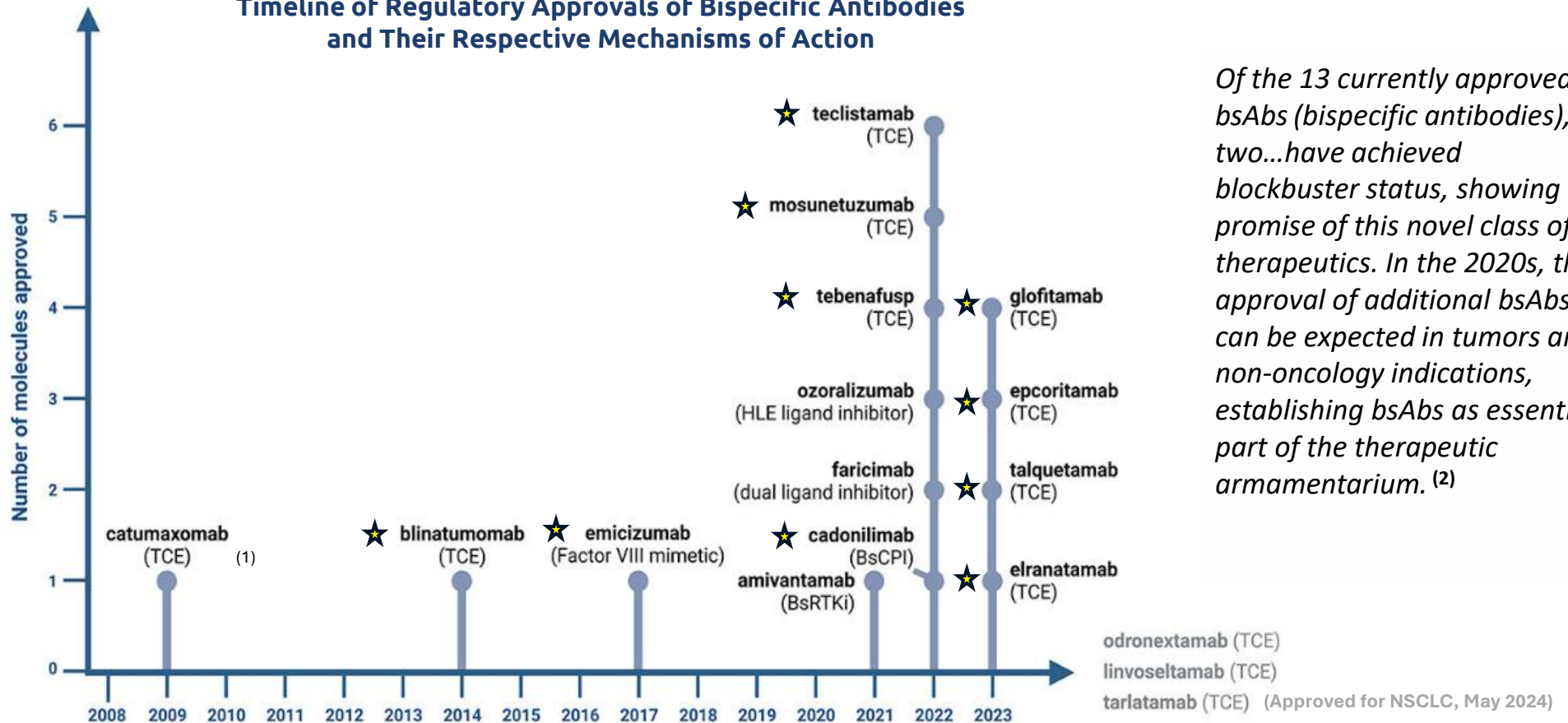
# Bispecifics Are Having Their Day

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 tumors and non-oncology indications, establishing bsAbs as essential part of the therapeutic armamentarium. (2)

★ Oncology related (1) No longer commercially marketed TCE = T Cell Engager

Source: A Pivotal Decade for Bispecific Antibodies? March 11, 2024

(2) A Pivotal Decade for Bispecific Antibodies?

# Aptevo's Differentiated & Diversified Bispecifics

- **Built to Overcome Common Safety Challenges**
- **Unique CD3 designed to reduce cytokine release syndrome (CRS)** as seen in prior mipletamig 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. radio isotopes, antibody drug conjugates (ADC's), adaptive T cells, checkpoint molecules, other bispecifics)
- CHO production cell lines used with antibody-like purification

# Diversified Pipeline Offers Multiple Opportunities for Partnering

	PROGRAM (Target)	POTENTIAL INDICATION(S)	PRECLINICAL	PHASE 1 (First-in-Human)	PHASE 2	NOTES
CLINICAL PROGRAMS	<b>Mipletamig (Formerly APVO436)</b> (CD3 x CD123)	Frontline AML				<b>RAINIER Phase 1/2 frontline AML trial underway*</b> <b>Orphan Drug Designation</b>
	<b>ALG.APV-527**</b> (4-1BB x 5T4)	NSCLC, Head & Neck, Colorectal, Pancreatic, Breast, Other Solid Tumors				Phase 1 trial ongoing, interim results 3Q24
PRE-CLINICAL PROGRAMS	<b>APVO711</b> (PD-L1 x CD40)	Multiple solid tumors				Preclinical studies ongoing
	<b>APVO603</b> (4-1BB x OX40)	Multiple solid tumors				IND enabling studies ongoing
	<b>APVO442</b> (PSMA x CD3)	Prostate Cancer				IND enabling studies ongoing

\*mipletamig combined with standard of care venetoclax + azacitidine in frontline patients

\*\*Partnered with Alligator Bioscience

# Market Opportunity

Aptevo is developing multiple molecules capable of targeting hematologic and solid tumor malignancies with large market potential



Select Global Market Opportunities*	Size
AML/MDS/Other leukemias	\$6.3B
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 2022



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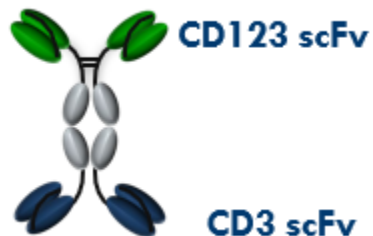
## Mipletamig AML, MDS and Other Leukemias

*“The mipletamig results are promising and show that it 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 Mipletamig for AML, MDS & Other Leukemias



## POTENTIAL INDICATIONS

Multiple blood cancers, including frontline and relapsed/refractory AML and MDS

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

## UNIQUE DESIGN

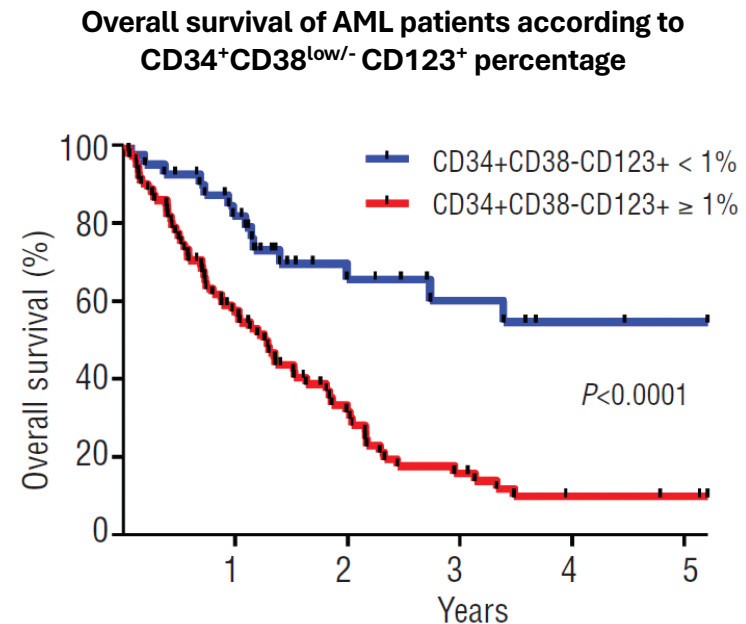
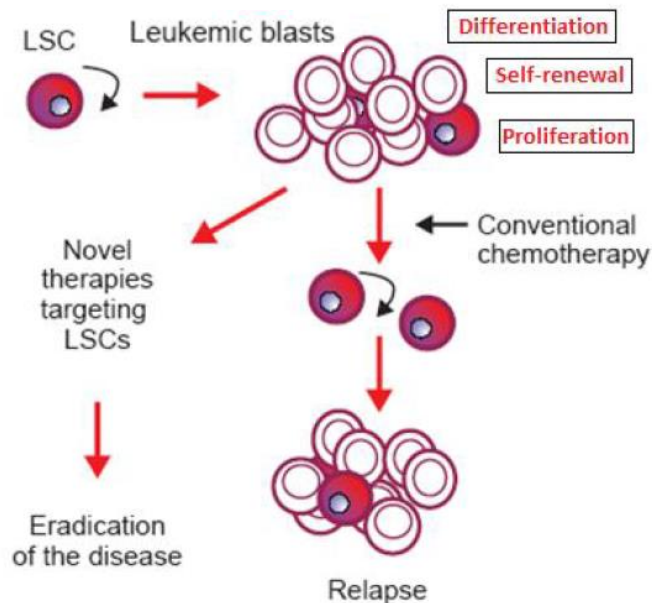
- Designed to engage T cells via CD3 binding to specifically kill CD123-expressing tumor cells. CD123 is a compelling target for AML due to its overexpression on leukemic stem cells and AML blasts
- Our CD3 binding domain is derived from CRIS-7; unique from competitors. Preclinical studies compared to 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

# 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



# Mipletamig: Trial Status and Results to Date

## Initiated: RAINIER Frontline AML Trial 3Q2024

### Part 1 of Phase 1b/2 in Frontline/Combination

- Evaluate up to 39 frontline AML patients who are not eligible for intensive induction due to age or other factors across five escalating dose level cohorts

### Primary Endpoints

- Evaluate the safety, tolerability, and maximum tolerated dose (MTD) of increasing doses of mipletamig in combination with venetoclax and azacitidine in patients with newly diagnosed AML
- Determine the recommended RP2D
- Assess incidence of cytokine release syndrome (CRS) at each dose level

### Secondary End point

- Determine efficacy at increasing doses of mipletamig in combination with venetoclax and azacitidine in patients with newly diagnosed AML



## Prior Outcomes: Compelling Results to Date

### Dose Escalation (monotherapy)

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

### Dose Expansion (combination therapy)

- 91% clinical benefit rate in combination with standard of care venetoclax + azacitidine in venetoclax naïve patients which is more than double our benchmark\*
  - 75% of frontline patients experienced a CR
- Clinically meaningful duration of remission, with no median reached – multiple patients either stayed on treatment or moved to transplant
- Only 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

Interim data readouts (open label) expected during 2H2024 & 1H2025

Part 1b dose optimization trial complete, preliminary data anticipated 1H2026

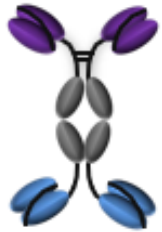


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by Design

**ALG.APV-527**

**Multiple Solid Tumor Type Expressing 5T4**

# Novel Bispecific ALG.APV-527 for Multiple Solid Tumors



$\alpha$ 4-1BB scFv

$\alpha$ 5T4 scFv

## 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

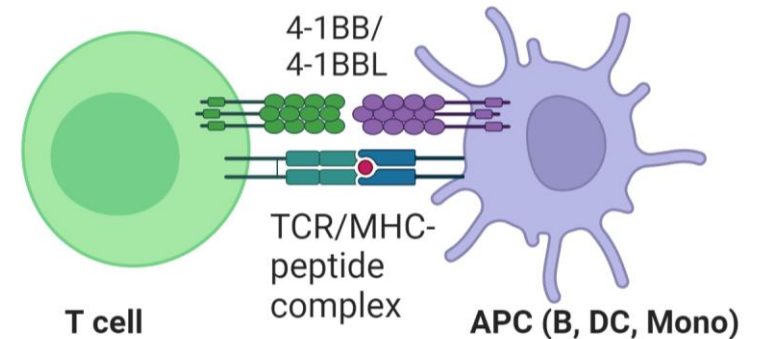
## Ownership

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

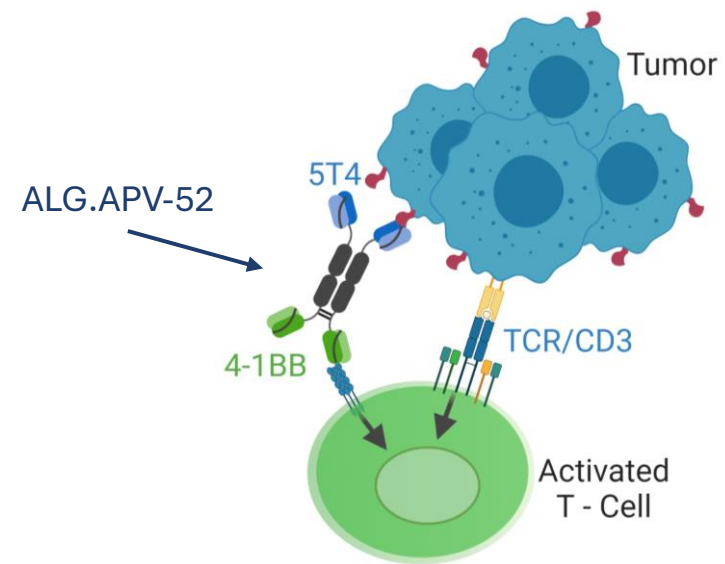
# Why We are Targeting 4-1BB + 5T4

- 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



# ALG.APV-527: Clinical Progress

## 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 and progressing breast cancer**. One patient remained on study for seven months with stable disease. The second patient remains on study with stable disease for more than 11 months and was safely transitioned higher dose levels twice

### Status

- Early trial data reported 1Q24
- Preliminary data anticipated 3Q24

## Upcoming Milestones

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



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## Preclinical Pipeline & Platforms



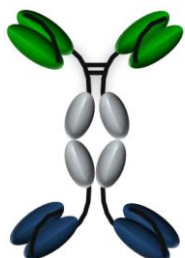
# Preclinical Pipeline: Novel, Solid Tumor-Targeted, Built for Safety

APV0711

APVO603

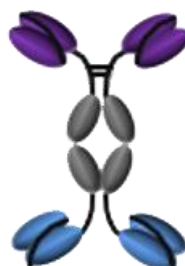
APVO442

## 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 radio isotopes



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# Wholly-Owned Proprietary Platforms

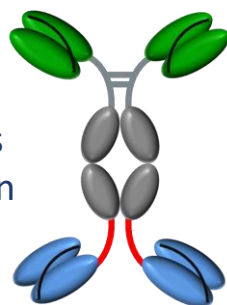
## ADAPTIR

### Drug Targeting

Bind up to two targets

### Genetic and Structural Format

Single gene that assembles into a homodimer based on an antibody backbone



Contains Immunoglobulin Gamma 1 Fc

### Half-life

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

### Manufacturing

Antibody-like manufacturing processes

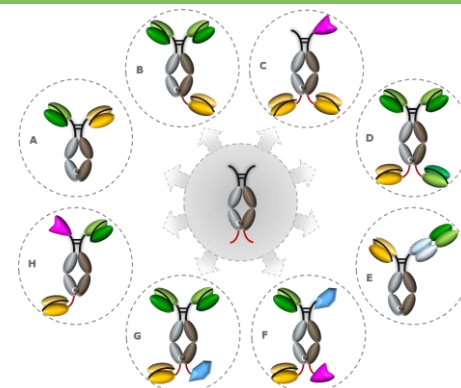
### Current Pipeline Candidates

Mipletamig (CD123 x CD3)  
 ALG.APV-527 (4-1BB x 5T4)  
 APVO603 (41BB x OX40)  
 APVO711 (PD-L1 x CD40)

## ADAPTIR-FLEX

Binds up to four targets

Two genes that assemble into a heterodimer with a knob-in-hole antibody backbone



Contains Immunoglobulin Gamma 1 Fc

Demonstrated antibody-like half-life in mice

Fc mutations may be utilized to eliminate binding to Fc Gamma Receptors or to enhance effector function

Antibody-like manufacturing processes

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

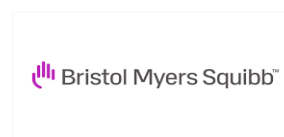
**Daniel Abdun-Nabi**, Director

**Grady Grant, III**, Director

**Marvin White**, Director

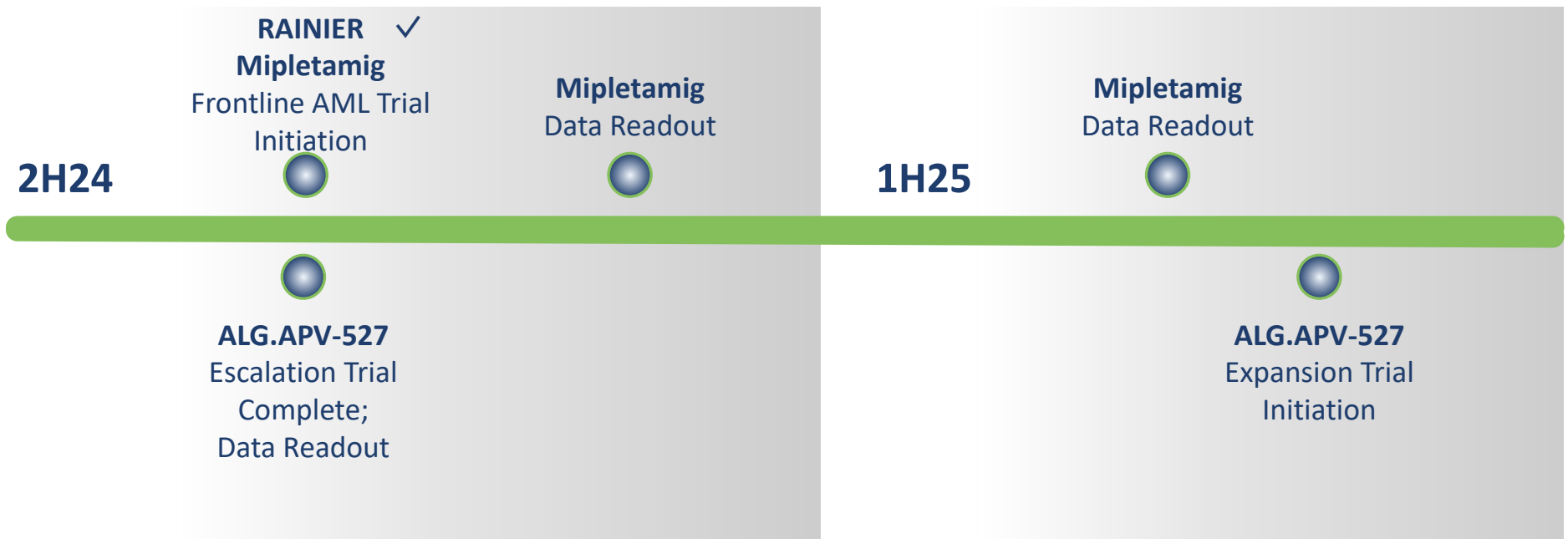


EMERGENT



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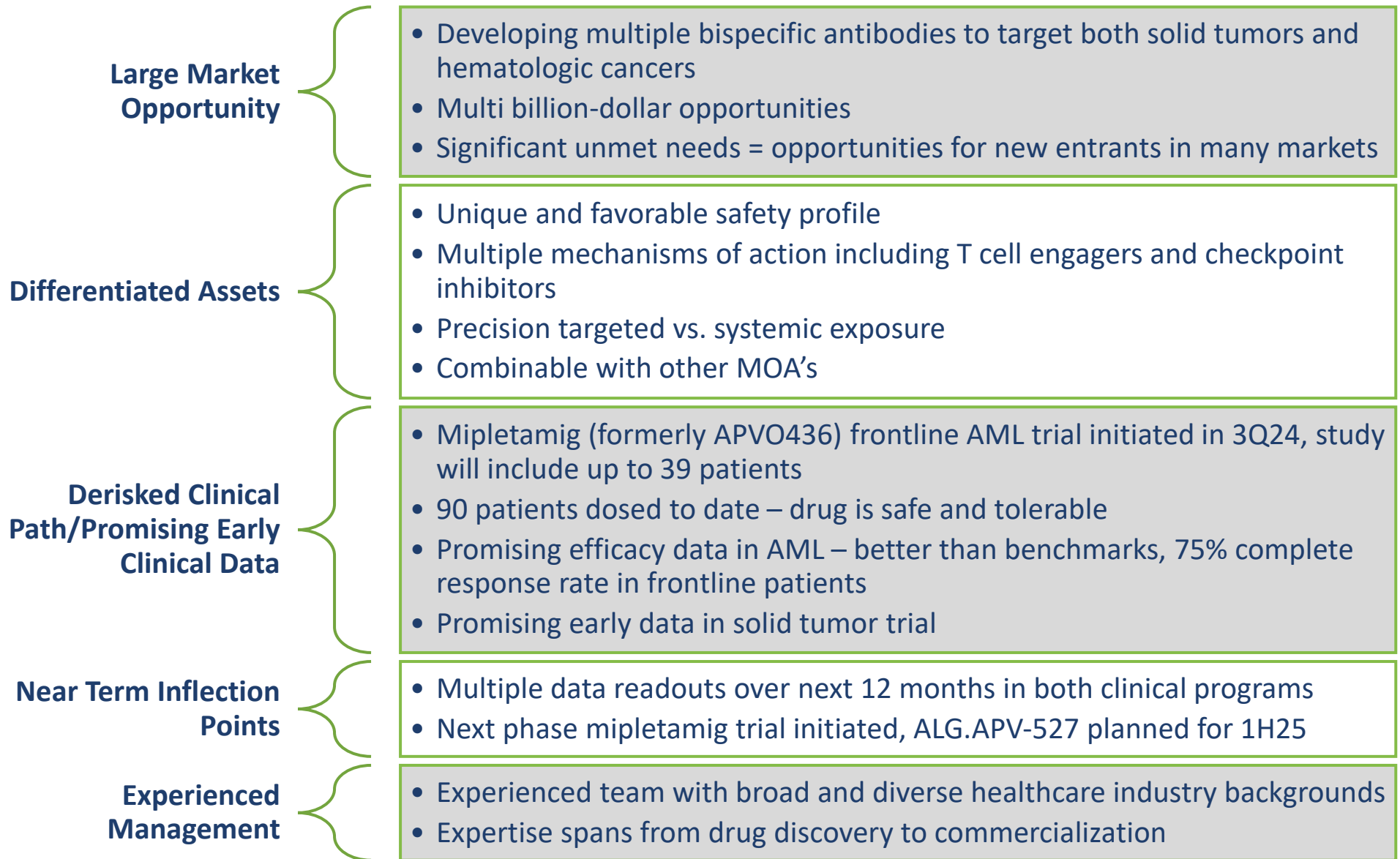
# Anticipated Milestones Through Mid-2025



*Multiple value-creating opportunities with two clinical drugs in development*

✓ *Initiated in August 2024*

# Investment Highlights





Thank You

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