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Aptevo Therapeutics Inc. (APVO-NASDAQ)

APVO: Initiating Coverage of Aptevo Therapeutics Inc.; Unlocking the Next Generation of Multispecific Immune Engagement

Based on our probability adjusted DCF model that takes into account potential future revenues for mipletamig and ALG.APV-527, Aptevo is valued at $30.00/share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based on future clinical results.

Current Price (06/16/26)	$4.84
Valuation	**$30.00**

OUTLOOK

We are initiating coverage of Aptevo Therapeutics Inc. (NASDAQ: APVO) with a $30.00 valuation. Aptevo is a clinical-stage immuno-oncology company focused on developing differentiated multispecific antibody therapeutics using its proprietary ADAPTIR and ADAPTIR-FLEX platform technologies. The company's lead clinical candidate, mipletamig, is a CD123 x CD3 bispecific T cell engager currently being evaluated in frontline acute myeloid leukemia (AML) in combination with venetoclax and azacitidine in the ongoing Phase 1b/2 RAINIER study. Initial clinical data generated to date suggest that mipletamig may possess a differentiated safety and tolerability profile relative to other CD3-engaging therapeutics targeting CD123, while still demonstrating encouraging anti-leukemic activity.

SUMMARY DATA

52-Week High	**$99.07**
52-Week Low	**$3.96**
One-Year Return (%)	**-94.15**
Beta	**1.64**
Average Daily Volume (sh)	**44,079**
Shares Outstanding (mil)	**1**
Market Capitalization ($mil)	**$6**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**8**
Insider Ownership (%)	**0**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2026 Estimate	**-0.2**
P/E using 2027 Estimate	**-0.2**

Risk Level	**Above Avg.**
Type of Stock	**Small-Value**
Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2025	0 A	0 A	0 A	0 A	0 A
2026	0 A	0 E	0 E	0 E	0 E
2027					0 E
2028					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2025	-$1581.73 A	-$151.29 A	-$40.13 A	-$7.26 A	-$87.27 A
2026	-$6.41 A	-$5.83 E	-$5.38 E	-$5.14 E	-$22.57 E
2027					-$2.78 E
2028					-$2.36 E

WHAT'S NEW

Initiating Coverage

Source: Aptevo Therapeutics, Inc.

We are initiating coverage of Aptevo Therapeutics Inc. (NASDAQ: APVO) with a valuation of $30.00. Aptevo is a clinical-stage biotechnology company developing multispecific immunotherapies designed to harness the immune system to selectively target and eliminate cancer cells. Aptevo's pipeline includes both hematologic malignancy and solid tumor programs built upon the company's proprietary ADAPTIR™ and ADAPTIR-FLEX™ platforms, which are engineered to generate bispecific and trispecific immune-engaging proteins with customizable functional characteristics.

The company's lead program, mipletamig, is a CD123 x CD3 bispecific T cell engager being evaluated for frontline acute myeloid leukemia (AML) in combination with venetoclax and azacitidine. Clinical data generated to date suggest that mipletamig may offer an attractive balance between efficacy and safety. Mipletamig is designed to reduce the risk of cytokine release syndrome (CRS), an often severe treatment toxicity and complication that can occur following therapy with bispecific antibodies.

Aptevo's broader pipeline includes several additional immune-engaging candidates targeting clinically validated tumor antigens and immune co-stimulatory pathways, including PSMA, Nectin-4, PD-L1, CD40, 4-1BB, and OX40. Importantly, many of these candidates incorporate the company's proprietary CRIS-7-derived CD3 binding domain, which management believes may contribute to a differentiated safety profile relative to competing CD3-engaging approaches.

Mipletamig Demonstrates Encouraging Frontline AML Data: Clinical data from frontline AML patients treated with mipletamig in combination with venetoclax and azacitidine demonstrated an 87% clinical benefit rate and 79% CR/CRi rate among evaluable patients. Importantly, no CRS has been observed among the frontline patient population through Cohort 5 of the RAINIER study.
Proprietary CRIS-7-Derived CD3 Binding Domain May Provide Differentiation: One of the most significant challenges associated with CD3-engaging bispecifics is CRS. Aptevo's proprietary CRIS-7-derived CD3 binding domain was specifically engineered to potentially reduce cytokine release while preserving anti-tumor activity.
ADAPTIR and ADAPTIR-FLEX Provide Broad Platform Utility: Aptevo's platform technologies enable the design of mono-, bi-, and trispecific therapeutics with customizable valency, immune activation, and half-life characteristics. This modularity may allow the company to efficiently generate multiple product candidates across diverse oncology indications.
Significant Unmet Need Remains Across Target Indications: AML remains an area of substantial unmet medical need despite the introduction of venetoclax-based frontline regimens. Similarly, solid tumor immunotherapy continues to face major challenges related to tumor localization, an immune suppressive tumor microenvironment (TME), and systemic toxicity.
Progression into Radiopharmaceutical Development with Niowave Collaboration: In May 2026, Aptevo announced a 50/50 collaboration with Niowave, Inc. to develop up to three radiopharmaceutical oncology programs, with Aptevo initially contributing Nectin-4 constructs. This collaboration is an important continuation of Aptevo's work with an emerging treatment paradigm.
Experienced Leadership Team with Deep Institutional Knowledge: Aptevo's senior management team has remained remarkably stable over time, with CEO Jeff Lam and CFO Daphne King serving since the company's formation and several other key executives contributing more than four years. We believe this continuity has fostered a cohesive operating culture and provided valuable institutional knowledge as the company has advanced both its ADAPTIR platform technologies and clinical pipeline.

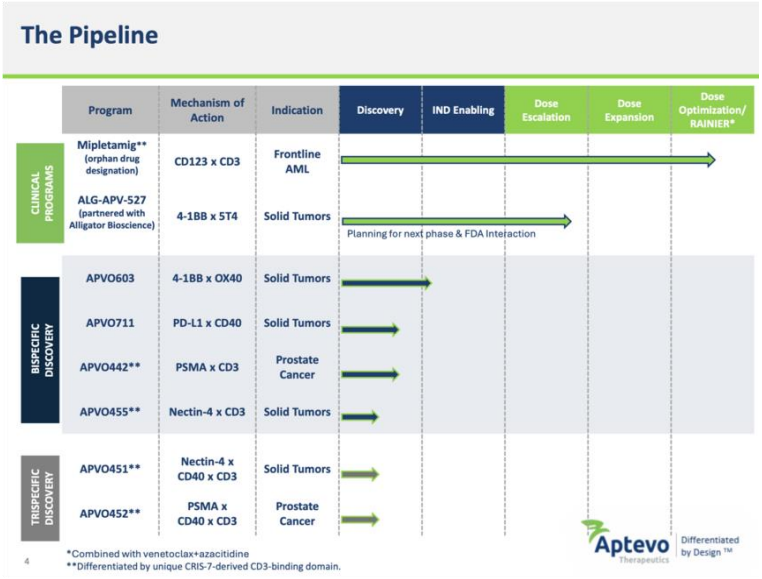
INVESTMENT THESIS

Aptevo Therapeutics is focused on the development of multispecific immunotherapies designed to engage and modulate the immune system for the treatment of cancer. The company's therapeutic approach centers around its proprietary ADAPTIR and ADAPTIR-FLEX platform technologies, which are capable of generating mono-, bi-, and trispecific immune-engaging proteins with customizable structural and functional properties.

We believe the company's investment thesis is driven primarily by the continued clinical validation of its CD3-engaging strategy in AML through mipletamig, combined with the broader optionality embedded within the ADAPTIR platform architecture.

Unlike many earlier-generation bispecific T-cell engagers, which were often limited by severe cytokine release syndrome and difficult dosing regimens, Aptevo's approach seeks to optimize the balance between immune activation and tolerability through rational molecular engineering. The company's lead clinical candidate, mipletamig, is specifically designed to target CD123-expressing leukemic cells while simultaneously engaging CD3-positive T cells. Importantly, the molecule incorporates a proprietary CRIS-7-derived CD3 binding domain that appears to reduce cytokine release while maintaining clinically meaningful anti-leukemic activity.

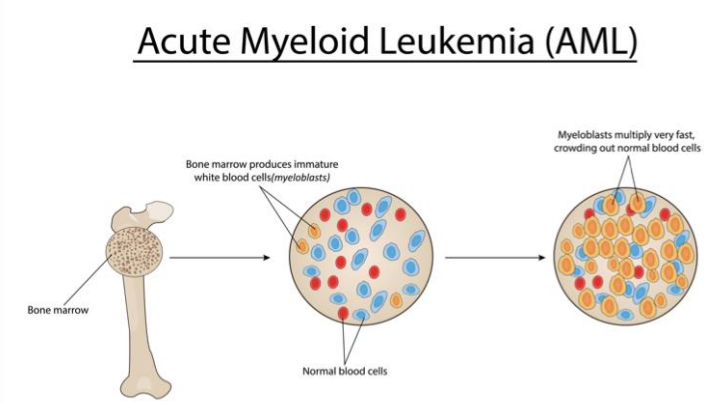
We believe this differentiated CD3 biology could ultimately prove highly important, as tolerability remains one of the central challenges limiting broader adoption and combinability of T-cell engaging therapies.



Source: Aptevo Therapeutics, Inc.

Acute Myeloid Leukemia (AML)

Acute myeloid leukemia (AML) is an aggressive hematologic malignancy characterized by the uncontrolled proliferation and impaired differentiation of immature myeloid precursor cells within the bone marrow and peripheral blood (Döhner *et al*., 2022). The disease results in progressive bone marrow failure, leading to anemia, thrombocytopenia, neutropenia, recurrent infections, and bleeding complications. AML represents the most common acute leukemia in adults and remains associated with poor long-term survival despite substantial advances in molecular diagnostics and targeted therapeutics over the past decade (Siegel *et al*., 2025).



Source: Shutterstock.com

The incidence of AML increases significantly with age. The median age at diagnosis in the United States is approximately 68 years, with the majority of cases occurring in patients over the age of 60 (Shallis *et al.*, 2019). According to the American Cancer Society, approximately 21,000 new AML cases and more than 11,000 AML-related deaths are expected annually in the United States alone (Siegel *et al.*, 2025). Outcomes remain particularly poor in older patients due to adverse cytogenetics, increased comorbidities, reduced tolerance for intensive chemotherapy, and higher rates of treatment resistance (Ferrara *et al.*, 2013).

AML is not a single disease entity but rather a highly heterogeneous collection of molecularly distinct malignancies driven by diverse genomic and epigenetic abnormalities. Recurrent mutations involving FLT3, NPM1, DNMT3A, IDH1, IDH2, TP53, RUNX1, ASXL1, TET2, and spliceosome-associated genes contribute to leukemogenesis through dysregulation of proliferation, apoptosis, differentiation, and stem-cell self-renewal pathways (Papaemmanuil *et al.*, 2016). This molecular heterogeneity has important prognostic and therapeutic implications and has increasingly driven the evolution toward precision medicine approaches in AML treatment.

Historically, frontline AML therapy was dominated by intensive induction chemotherapy, most commonly consisting of cytarabine combined with an anthracycline ("7+3" therapy), which remained the standard-of-care for decades (Yates *et al.*, 1973). While intensive induction can produce complete remission rates approaching 60-80% in younger fit patients, outcomes remain substantially worse in elderly patients and those with adverse-risk disease biology (Dombret *et al.*, 2016). Furthermore, relapse following initial remission remains common due to the persistence of chemotherapy-resistant leukemic stem cells (LSCs), which are believed to drive disease recurrence and therapeutic resistance (Jordan *et al.*, 2006).

The AML treatment landscape has changed dramatically over the last decade with the introduction of multiple targeted therapies and lower-intensity combination regimens. Among the most important advances was the development of venetoclax, a potent and selective BCL-2 inhibitor that restores apoptotic signaling in leukemic cells (Konopleva *et al.*, 2016). In the landmark Phase 3 VIALE-A study, venetoclax combined with azacitidine demonstrated significant improvements in complete remission rates, overall survival, and event-free survival compared to azacitidine alone in newly diagnosed AML patients who were ineligible for intensive induction chemotherapy (DiNardo *et al.*, 2020). The regimen rapidly became the frontline standard-of-care for older or medically unfit AML patients.

Despite the substantial advancement represented by venetoclax-based frontline regimens, major unmet medical needs remain in AML. Venetoclax combined with azacitidine has demonstrated high initial response rates in newly diagnosed elderly or medically unfit AML patients; however, the majority of patients ultimately relapse and long-term survival remains limited despite improved remission induction relative to azacitidine alone (DiNardo *et al.*, 2020). Increasing evidence suggests that resistance to venetoclax-based therapy is driven by multiple adaptive mechanisms, including metabolic reprogramming of leukemic stem cells, altered mitochondrial energetics, and compensatory dependence on alternative anti-apoptotic pathways such as MCL-1 and BCL-XL (Stevens *et al.*, 2020; Nachmias *et al.*, 2024).

Importantly, venetoclax-based regimens appear less effective in biologically adverse AML subsets, including patients harboring TP53 mutations, secondary AML, therapy-related AML, or complex cytogenetic abnormalities, all of which continue to demonstrate poor overall survival and limited remission durability despite recent therapeutic advances (Döhner *et al*., 2022; Nechiporuk *et al*., 2019; DiNardo *et al*., 2020). These limitations have intensified interest in novel combination strategies capable of improving remission depth, overcoming resistance biology, and more effectively eradicating leukemic stem-cell populations.

The emergence of measurable residual disease (MRD) as a clinically important biomarker has further highlighted the limitations of current therapies. Numerous studies have demonstrated that persistence of MRD following treatment is strongly associated with relapse risk and inferior survival outcomes (Hourigan *et al*., 2013). Consequently, there is growing interest in therapeutic approaches capable of producing deeper remissions and more effective eradication of leukemic stem-cell compartments.

One of the most intensively investigated therapeutic targets in AML is CD123, the alpha chain of the interleukin-3 receptor (IL-3Rα). CD123 is highly expressed on AML blast cells and leukemic stem cells while demonstrating relatively limited expression on normal hematopoietic stem cells, creating a potentially attractive therapeutic window (Jordan *et al*., 2000). Importantly, elevated CD123 expression has been associated with poor prognosis, increased proliferative capacity, and adverse disease biology in AML patients (Testa *et al*., 2002; Vergez *et al*., 2011).

The biological importance of leukemic stem cells in AML cannot be overstated. Unlike bulk leukemic blasts, leukemic stem cells possess the ability to self-renew, evade chemotherapy-induced apoptosis, and reconstitute disease following treatment (Bonnet *et al*., 1997). Increasing evidence suggests that durable disease control in AML may ultimately require effective targeting of these stem-cell populations in addition to cytoreduction of bulk leukemic burden. Because CD123 is enriched on leukemic stem cells, therapies directed against CD123 have attracted substantial interest as potentially disease-modifying approaches.

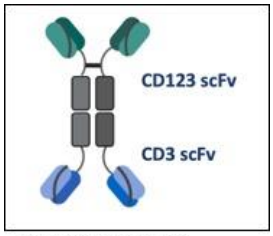
Multiple CD123-targeting strategies are currently under development, including monoclonal antibodies, antibody-drug conjugates (ADCs), CAR-T therapies, NK-cell engagers, and bispecific T cell engagers (Ehninger *et al*., 2014). Among these approaches, bispecific CD123 x CD3 T cell engagers have emerged as particularly promising due to their ability to redirect endogenous cytotoxic T cells toward leukemic targets independent of peptide-MHC presentation (Baeuerle *et al*., 2009).

However, the development of CD3-engaging therapies has been associated with significant challenges, most notably cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) (Shimabukuro-Vornhagen *et al*., 2018). CRS results from rapid immune activation and massive inflammatory cytokine release following T cell engagement and can range from mild constitutional symptoms to life-threatening hypotension, respiratory failure, and multiorgan dysfunction. These toxicities have represented major limitations for many first-generation T cell engagers and CAR-T therapies, particularly in older AML populations with substantial comorbidity burdens.

Consequently, substantial effort within the field has focused on engineering next-generation bispecific molecules capable of preserving anti-tumor activity while reducing excessive cytokine release and improving tolerability profiles. This has become one of the central strategic differentiators within the broader bispecific T cell engager landscape.

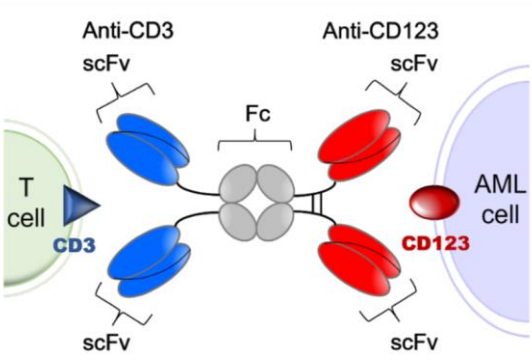
Mipletamig

Mipletamig is Aptevo's lead clinical-stage immunotherapy candidate and currently represents the company's primary value driver. The molecule is a CD123 x CD3 bispecific T cell engager generated using the company's proprietary ADAPTIR platform and was specifically engineered to redirect endogenous cytotoxic T cells toward leukemic blasts and leukemic stem cells expressing CD123. Unlike many



Source: Aptevo Therapeutics, Inc.

earlier-generation T cell engagers that utilized highly potent CD3-binding domains associated with substantial CRS, mipletamig incorporates Aptevo's proprietary CRIS-7-derived CD3 binding domain, which was designed to preserve anti-leukemic activity while reducing excessive immune activation and inflammatory cytokine release. In our view, this engineered balance between efficacy and tolerability represents one of the most important differentiating features of the program.



Source: Aptevo Therapeutics, Inc.

The rationale for combining mipletamig with venetoclax and azacitidine is scientifically compelling. While venetoclax plus azacitidine has significantly improved remission rates relative to hypomethylating agents alone, most patients eventually relapse, and durable long-term remissions remain uncommon. Aptevo's strategy seeks to augment venetoclax-induced leukemic apoptosis through simultaneous immune-mediated cytotoxic elimination of residual leukemic cells and leukemic stem-cell populations via T cell redirection.

Mipletamig has now been evaluated across multiple clinical studies, including early monotherapy dose-escalation trials, dose-expansion studies, and the ongoing Phase 1b/2 RAINIER frontline AML trial. Collectively, the molecule has been administered to more than 120 patients to date, providing a meaningful emerging safety database for a CD3-engaging therapy in AML. Importantly, the program has consistently demonstrated encouraging anti-leukemic activity alongside what appears to be a differentiated tolerability profile relative to many competing CD123-directed T cell engager programs.

Initial clinical proof-of-concept for mipletamig was established during the Phase 1 dose-escalation and dose-expansion studies conducted in relapsed/refractory AML and myelodysplastic syndrome (MDS) patients (NCT03647800). This was a two-part, Phase 1a/b dose-escalation and expansion study with the goal of evaluating the safety and tolerability of mipletamig (APVO436) when used as a monotherapy and in combination therapy modalities. In December 2022, the company reported that of a total of 16 response-evaluable patients that received the combination therapy of venetoclax and azacytidine with mipletimag, 75% experienced clinical benefit while 100% of patients in that cohort who had not received venetoclax previously experienced clinical benefit, which included a complete remission (CR), complete remission with incomplete hematologic recovery (CRi), or morphologic leukemia-free state (MLFS). Importantly, CRS events observed in this study were generally low grade and manageable, supporting the underlying hypothesis that the CRIS-7-derived CD3 binding domain may attenuate excessive cytokine signaling relative to more potent CD3-binding approaches.

Based on these results, the program subsequently transitioned toward frontline AML combination therapy, where Aptevo believes the molecule may possess its greatest commercial and clinical opportunity. The ongoing RAINIER study is a Phase 1b/2, multi-center, open-label trial evaluating mipletamig in combination with venetoclax and azacitidine in newly diagnosed AML patients who are ineligible for intensive induction chemotherapy (NCT06634394). The trial is designed as a dose-optimization study intended to identify the recommended Phase 2 dose (RP2D) while simultaneously generating preliminary efficacy and safety data across escalating dose cohorts.

In May 2026, Aptevo released the most recent RAINIER update, which included data from 31 evaluable frontline AML patients treated through Cohort 5, including 27 patients enrolled in RAINIER and four

additional patients from the prior dose-expansion study. The results were highly encouraging and, in our view, represent the strongest dataset generated to date for the program. Across the evaluable population, mipletamig in combination with venetoclax and azacitidine produced an 87% clinical benefit rate, defined as complete remission (CR), complete remission with incomplete hematologic recovery (CRi), or partial remission (PR). Most notably, 81% of patients achieved CR/CRi, while 65% achieved complete remission.

These response rates compare favorably to historical outcomes reported in VIALE-A, where venetoclax plus azacitidine alone generated a CR/CRi rate of approximately 66% and a CR rate of 37% in frontline AML patients unfit for intensive induction chemotherapy (DiNardo *et al.*, 2020). While important caveats regarding cross-trial comparisons clearly apply, the magnitude of improvement observed thus far in RAINIER appears potentially clinically meaningful.

Endpoint	RAINIER (Mipletamig + Venetoclax + Azacitidine)	VIALE-A (Venetoclax + Azacitidine)	Potential Interpretation
Patient Population	Newly diagnosed AML patients unfit for intensive induction chemotherapy	Newly diagnosed AML patients unfit for intensive induction chemotherapy	Broadly similar frontline AML setting
Evaluable Patients	31	286	RAINIER dataset remains early and substantially smaller
Clinical Benefit Rate	87%	Not formally reported as "clinical benefit rate"	Suggests broad anti-leukemic activity
CR/CRi Rate	81%	~66%	Potentially improved remission induction
Complete Remission (CR) Rate	65%	~37%	Numerically favorable relative to historical controls
MRD-Negative Responses	~55% among CR/CRi patients	Lower MRD negativity rates historically reported	Potentially deeper remissions
Activity in TP53-Mutated AML	Responses observed in TP53-mutated patients	TP53-mutated AML historically associated with poor durability	Important area for future validation
Cytokine Release Syndrome (CRS)	No CRS reported to date in frontline patients	Not applicable (non-CD3 therapy)	Potentially important differentiation versus competing bispecifics
Mechanistic Approach	BCL-2 inhibition + hypomethylation + T cell redirection	BCL-2 inhibition + hypomethylation	Addition of immune-mediated leukemic cell killing
Potential Differentiator	Combines frontline backbone therapy with CD123-directed immune engagement	Established frontline standard-of-care	Potential for improved remission depth and stem-cell targeting

*Cross-trial comparisons are inherently limited by differences in study design, patient selection, sample size, follow-up duration, and response assessment methodologies. The RAINIER dataset remains early-stage and requires additional clinical validation.

Sources: DiNardo et al., 2020; Aptevo Therapeutics, Inc.

Particularly noteworthy was the emergence of measurable residual disease (MRD)-negative responses within the study population. Among patients achieving CR/CRi, approximately 55% reached MRD-negative status. MRD negativity has increasingly emerged as one of the strongest prognostic biomarkers in AML and is generally associated with improved remission durability and overall survival outcomes. In our view, the ability to generate MRD-negative remissions may ultimately represent one of the more important indicators supporting the biologic activity of mipletamig within frontline AML.

Another highly important observation from the RAINIER study involves activity in TP53-mutated AML patients. Approximately 36% of remission patients harbored TP53 mutations, which represent one of the most difficult-to-treat and highest-risk AML subgroups. TP53-mutated AML is historically associated with extremely poor prognosis, resistance to conventional chemotherapy, inferior venetoclax durability, and poor overall survival (Welch *et al.*, 2016). Although patient numbers remain small, evidence of remission activity within this subgroup may ultimately prove clinically meaningful if validated in larger studies.

Perhaps the most differentiating aspect of the RAINIER dataset to date is the apparent safety profile. Importantly, no CRS has been reported in frontline AML patients treated through Cohort 5 of the RAINIER study. This observation is potentially highly significant within the broader context of T cell engager development. CRS remains one of the central limitations associated with CD3-engaging immunotherapies and has historically complicated development of multiple competing CD123-directed bispecifics, particularly in older AML populations with substantial comorbidity burdens (Shimabukuro-Vornhagen *et al.*, 2018). The absence of CRS observed thus far may support management's thesis that the CRIS-7-derived CD3 binding domain meaningfully modulates immune activation while preserving anti-tumor cytotoxicity.

The ability to combine a CD3-engaging bispecific with standard venetoclax plus azacitidine therapy without substantially exacerbating toxicity could prove commercially and clinically important. Frontline AML patients who are elderly or medically unfit frequently possess limited physiologic reserve, making

tolerability a critical determinant of therapeutic adoption. In this context, the emergence of strong efficacy signals without apparent additive CRS burden may represent one of mipletamig's most important competitive differentiators.

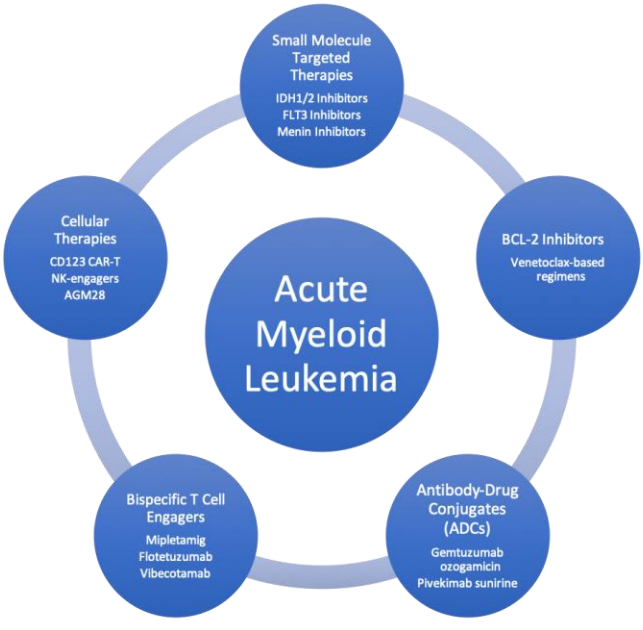
The RAINIER study has now progressed into its final dose-optimization stage, including Cohorts 6 and 7, which represent the highest mipletamig dose levels evaluated to date. Aptevo expects the study to support selection of a recommended Phase 2 dose by the end of 2026. In our view, additional maturation of the RAINIER dataset, particularly regarding durability of remission, MRD persistence, transplant outcomes, and overall survival trends, will represent important future catalysts for the program.

Although the data generated to date remain early and patient numbers remain limited, we believe mipletamig is increasingly emerging as one of the more differentiated CD123-directed T cell engager programs currently in clinical development. The combination of encouraging remission activity, MRD-negative responses, apparent activity in biologically adverse AML subsets, and the absence of CRS observed thus far collectively support continued advancement of the program.

AML Competitive Landscape

The treatment landscape for AML has evolved dramatically over the last decade, transforming from one dominated almost exclusively by intensive cytotoxic chemotherapy into an increasingly molecularly stratified and immunologically targeted therapeutic market. Historically, treatment options for AML remained largely unchanged for more than 40 years following the establishment of cytarabine plus anthracycline ("7+3") induction chemotherapy in the 1970s. However, improvements in genomic characterization, disease biology, and immuno-oncology have catalyzed the development of multiple targeted therapies, antibody-based approaches, cellular therapies, and next-generation combination regimens aimed at improving remission durability and overall survival.

The modern AML market is now increasingly segmented across several major therapeutic categories, including FLT3 inhibitors, IDH inhibitors, BCL-2 inhibitors, antibody-drug conjugates, menin inhibitors, macrophage checkpoint inhibitors, bispecific T cell engagers, NK cell engagers, and cellular immunotherapies. Importantly, despite recent approvals, relapse rates remain high across essentially all frontline regimens, creating continued opportunity for novel therapeutic approaches capable of improving remission depth, overcoming resistance mechanisms, and more effectively eradicating leukemic stem-cell populations.



Source: Zacks SCR

The most commercially important advancement in frontline AML therapy over the last decade has been the emergence of venetoclax-based regimens. Venetoclax, a selective BCL-2 inhibitor originally developed by AbbVie and Roche, fundamentally altered the treatment paradigm for elderly or medically unfit AML patients following the Phase 3 VIALE-A trial. In VIALE-A, venetoclax combined with azacitidine demonstrated significantly improved complete remission rates and median overall survival relative to azacitidine alone, ultimately establishing the combination as frontline standard-of-care therapy for patients ineligible for intensive induction chemotherapy (DiNardo *et al*., 2020). The study reported median overall survival of 14.7 months for venetoclax plus azacitidine versus 9.6 months for azacitidine monotherapy, while CR/CRi rates improved to approximately 66% compared to 28% with azacitidine alone. Despite these improvements, long-term outcomes remain suboptimal, particularly in TP53-mutated AML and secondary AML populations, and relapse following initial response remains common.

The FLT3-mutated AML subset has also undergone substantial therapeutic evolution. FLT3 mutations occur in approximately 30% of AML cases and are generally associated with aggressive disease biology and poor prognosis (Papaemmanuil *et al*., 2016). Novartis' midostaurin became the first FLT3 inhibitor approved for AML following the RATIFY trial, which demonstrated improved overall survival when added to standard induction chemotherapy in newly diagnosed FLT3-mutated AML patients (Stone *et al*., 2017). More recently, second-generation FLT3 inhibitors including gilteritinib and quizartinib have demonstrated additional clinical activity in both relapsed/refractory and frontline settings. In the ADMIRAL study, gilteritinib significantly improved median overall survival versus salvage chemotherapy in relapsed/refractory FLT3-mutated AML, supporting its approval in the post-relapse setting (Perl *et al*., 2019). Quizartinib subsequently demonstrated improved overall survival in newly diagnosed FLT3-ITD AML patients in the QuANTUM-First trial, further solidifying FLT3 inhibition as a major AML treatment backbone (Erba *et al*., 2023).

Targeted inhibition of mutant IDH enzymes has similarly become an established component of AML therapy. Mutations in IDH1 and IDH2 collectively occur in approximately 15-20% of AML patients and promote leukemogenesis through production of the oncometabolite 2-hydroxyglutarate, resulting in epigenetic dysregulation and impaired differentiation (Papaemmanuil *et al*., 2016). Servier and Bristol Myers Squibb's IDH inhibitors ivosidenib and enasidenib demonstrated meaningful single-agent activity in relapsed/refractory AML and subsequently expanded into frontline combination settings (Stein *et al*., 2017; Montesinos *et al*., 2022). However, while IDH inhibitors produce durable responses in selected patients, resistance and clonal evolution remain substantial limitations.

The antibody-drug conjugate (ADC) market in AML has also continued to evolve. Pfizer's gemtuzumab ozogamicin, a CD33-targeting ADC, was initially approved in 2000, later withdrawn due to toxicity concerns, and subsequently reapproved following demonstration of improved event-free survival using fractionated dosing schedules (Castaigne *et al*., 2012). More recently, next-generation ADCs targeting CD123 have entered development, including pivekimab sunirine (IMGN632), originally developed by ImmunoGen prior to its acquisition by AbbVie. Early studies demonstrated encouraging activity with an improved therapeutic window relative to earlier CD123-targeting ADCs, although hematologic toxicity remains a challenge (Daver *et al*., 2024).

One of the most rapidly evolving areas within AML therapeutics is the development of immune-based therapies targeting leukemic antigens including CD123, CD33, CLL-1, and FLT3. Among these, CD123-directed approaches have attracted particularly strong interest due to the antigen's expression on leukemic stem-cell populations. Several CD123-directed bispecific T-cell engagers are currently in development. MacroGenics' flotetuzumab, a CD123 x CD3 DART molecule, demonstrated anti-leukemic activity in relapsed/refractory AML, particularly in primary induction failure and early relapse populations (Uy *et al*., 2021). However, development of flotetuzumab has been complicated by CRS and immune-related toxicities that remain common across many first-generation CD3-engaging therapies.

Similarly, Xencor's vibecotamab (XmAb14045), another CD123 x CD3 bispecific, demonstrated encouraging early remission activity in relapsed/refractory AML, although CRS remained frequent and represented a significant management consideration (Ravandi *et al*., 2023). In our view, the challenges

encountered across competing CD123 bispecific programs highlight the central importance of balancing immune activation with tolerability, particularly in elderly AML populations with substantial comorbidity burdens.

Natural killer (NK) cell-engaging therapies have also emerged as a potentially differentiated immunotherapy modality within AML. Affimed's AFM28, a CD123 x CD16A innate cell engager, seeks to activate endogenous NK cells rather than T cells, potentially reducing CRS relative to CD3-engaging approaches. Early clinical development remains ongoing, and it remains unclear whether NK-cell engagement can achieve efficacy comparable to T cell redirection in AML.

Menin inhibition has more recently emerged as one of the most important new targeted approaches in AML. This therapeutic strategy is increasingly important for the genomically defined subset of patients that harbor KMT2A rearrangements (~5%) and NPM1 mutations (~30%) (Uckelmann *et al*., 2020). Menin inhibitors disrupt the interaction between menin and KMT2A-rearranged or NPM1-mutated leukemic transcriptional complexes, thereby restoring differentiation programs within leukemic cells. Syndax Pharmaceuticals' revumenib generated highly encouraging response rates in relapsed/refractory KMT2A-rearranged leukemias and received substantial attention following publication of the AUGMENT-101 dataset (Issa *et al*., 2025). Similarly, Kura Oncology and Kyowa Kirin's ziftomenib has demonstrated promising activity in NPM1-mutated AML and remains in ongoing development. Menin inhibition may ultimately become a major targeted therapy class within genomically defined AML subsets.

Cellular therapies remain an area of intense development interest but have encountered substantial challenges in AML relative to B-cell malignancies. Unlike CD19-directed CAR-T therapies in lymphoma and leukemia, AML lacks an ideal lineage-restricted antigen that can be targeted without causing prolonged myeloablation and marrow toxicity. Multiple CD123-directed, CLL-1-directed, and CD33-directed CAR-T programs remain in development; however, issues surrounding antigen heterogeneity, prolonged cytopenias, manufacturing complexity, and CRS continue to complicate development (Vishwasrao *et al*., 2022).

The following table provides an overview of the AML competitive landscape, which remains highly dynamic and increasingly crowded across both targeted therapy and immunotherapy treatments. While there have been many recent approvals, durable long-term disease control remains elusive for most AML patients, particularly in elderly frontline populations and biologically adverse disease subsets. We believe this continued unmet need creates opportunity for differentiated therapies capable of improving remission depth and durability while maintaining acceptable tolerability profiles. Thus, we believe mipletamig's emerging profile may position the molecule competitively within the broader CD123-directed immunotherapy landscape. The combination of encouraging remission activity, MRD-negative responses, apparent activity in TP53-mutated AML, and the absence of CRS reported to date in frontline patients may represent meaningful differentiators if validated in larger clinical studies.

Competitive Landscape of Approved and Emerging AML Therapies

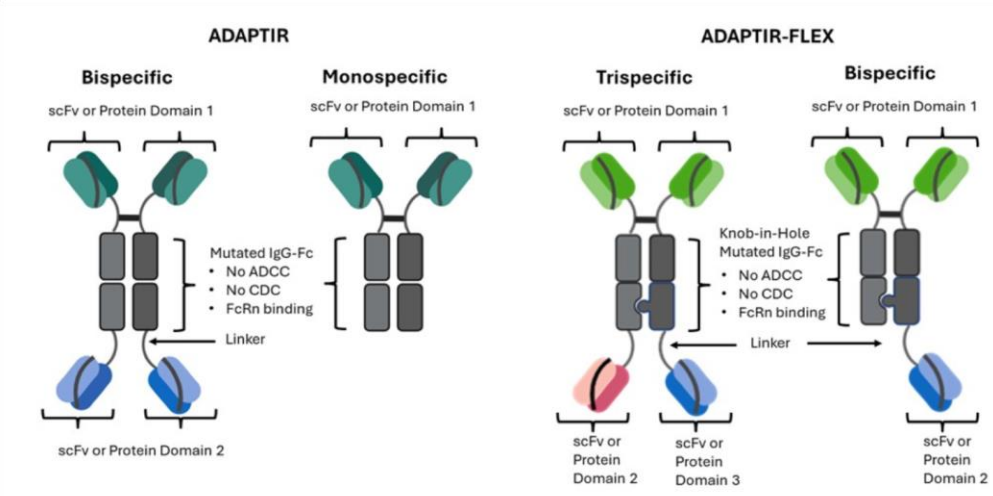
Therapy	Company	Target / Mechanism	AML Setting	Key Trial	Key Outcomes	Major Limitations
Venetoclax + Azacitidine	AbbVie/Roche	BCL-2 inhibition	Frontline unfit AML	VIALE-A	OS benefit; CR/CRi ~66%	Relapse, cytopenias
Mipletamig	Aptevo	CD123 x CD3 bispecific	Frontline AML	RAINIER	81% CR/CRi; no CRS reported	Early-stage dataset
Flotetuzumab	MacroGenics	CD123 x CD3 bispecific	R/R AML	Early Phase Studies	Anti-leukemic activity	CRS
Vibecotamab	Xencor	CD123 x CD3 bispecific	R/R AML	Phase 1	CR activity	CRS
Midostaurin	Novartis	FLT3 inhibitor	Frontline FLT3 AML	RATIFY	OS improvement	Resistance mutations
Gilteritinib	Astellas	FLT3 inhibitor	R/R FLT3 AML	ADMIRAL	Improved OS	Relapse/resistance
Quizartinib	Daiichi Sankyo	FLT3 inhibitor	Frontline FLT3-ITD AML	QuANTUM-First	OS improvement	QT prolongation
Ivosidenib	Servier	IDH1 inhibitor	IDH1 AML	AG120 studies	Durable responses	Resistance evolution
Enasidenib	BMS	IDH2 inhibitor	IDH2 AML	AG221 studies	Differentiation responses	Slow response kinetics
Gemtuzumab Ozogamicin	Pfizer	CD33 ADC	Frontline AML	ALFA-0701	Improved EFS	Hepatotoxicity
AFM28	Affimed	CD123 x CD16A engager	Early AML	Ongoing	Early development	Unproven efficacy
Revumenib	Syndax	Menin inhibitor	KMT2A AML	AUGMENT-101	High response activity	Resistance development
Ziftomenib	Kura/Kyowa Kirin	Menin inhibitor	NPM1 AML	KOMET studies	Promising activity	Early-stage

Sources: Company documents

ADAPTIR™/ADAPTIR-FLEX™ Platform and Pipeline Analysis

Aptevo has positioned its ADAPTIR™ and ADAPTIR-FLEX™ platforms as next-generation multispecific antibody engineering systems intended to address several of the central limitations historically associated with T cell engager and immunostimulatory biologic therapies. The broader bispecific antibody market has evolved rapidly over the last decade following the clinical validation of immune-cell redirecting therapies such as blinatumomab, teclistamab, mosunetuzumab, and epcoritamab, all of which demonstrated that simultaneous engagement of immune effector cells and tumor-associated antigens can generate potent anti-tumor activity across hematologic malignancies (Brinkmann *et al.*, 2017). However, despite the promise of the modality, many first-generation bispecific approaches have encountered substantial limitations related to CRS, short serum half-life, poor pharmacokinetics, aggregation risk, manufacturing complexity, and limited therapeutic windows (Spiess *et al.*, 2015). In response, substantial industry effort has focused on developing more structurally sophisticated multispecific architectures capable of improving stability, tumor selectivity, pharmacology, and immune tolerability.

The ADAPTIR platform was specifically engineered to address these challenges through a modular Fc-containing bispecific antibody architecture designed to support flexible target orientation, valency optimization, and improved manufacturability. Unlike smaller BiTE-like constructs lacking Fc regions, ADAPTIR molecules retain Fc-mediated structural support, which may improve serum half-life and pharmacokinetic properties while also supporting scalable manufacturing processes. The platform was also designed to permit selective tuning of CD3 affinity and immune synapse formation, which may be particularly important in minimizing excessive cytokine release while preserving anti-tumor cytotoxicity.



Source: Aptevo Therapeutics, Inc.

This latter point has become increasingly important across the broader T cell engager field. Many first-generation CD3-engaging molecules demonstrated strong anti-tumor activity but also generated clinically significant CRS and immune effector neurotoxicity, particularly in heavily pretreated hematologic malignancy populations. Aptevo's engineering strategy appears specifically focused on modulating immune activation intensity through careful CD3 binding optimization. The company's proprietary CRIS-7-derived CD3 binding domain, incorporated into mipletamig and several next-generation pipeline candidates, was designed to preserve effective T cell-mediated tumor killing while potentially reducing systemic inflammatory signaling.

The company subsequently expanded the platform through development of ADAPTIR-FLEX, a more structurally sophisticated heterodimeric, multispecific architecture designed to support tetravalent and trispecific therapeutic molecules. ADAPTIR-FLEX utilizes heterodimeric heavy-chain engineering that allows incorporation of multiple independent binding domains into a single therapeutic construct while maintaining manufacturability and molecular stability. In our view, this evolution toward increasingly

complex multispecific architectures reflects broader industry movement toward therapies capable of integrating tumor targeting, immune co-stimulation, checkpoint inhibition, and conditional immune activation within a single molecule.

A particularly important strategic feature of the ADAPTIR-FLEX platform is its emphasis on conditional immune activation. Several pipeline candidates are specifically designed to activate immune signaling pathways only in the presence of tumor-associated antigen binding, thereby potentially localizing immune activation to the tumor microenvironment while reducing systemic toxicity. This concept has become increasingly attractive within immuno-oncology following historical safety challenges associated with systemic immune agonists, particularly 4-1BB agonists, which demonstrated hepatotoxicity and inflammatory toxicity in early clinical studies (Segal *et al.*, 2017). In our view, tumor-localized co-stimulation may represent one of the more important next-generation themes emerging within multispecific immunotherapy development.

Importantly, the ADAPTIR and ADAPTIR-FLEX platforms have already generated multiple clinical-stage and preclinical assets spanning both hematologic malignancies and solid tumors. The breadth of the pipeline demonstrates the flexibility of the platform architecture and highlights the company's strategy of leveraging common engineering principles across multiple immunotherapy candidates. In addition to mipletamig, which was discussed earlier, the pipeline includes:

ALG.APV-527 (4-1BB x 5T4; Solid Tumors)
ALG.APV-527 represents Aptevo's second clinical-stage asset and was developed in collaboration with Alligator Bioscience using the ADAPTIR-FLEX platform. The molecule is a tumor-directed 4-1BB agonistic bispecific antibody targeting both 4-1BB (CD137) and 5T4. 4-1BB is a potent co-stimulatory receptor expressed on activated T cells and NK cells that enhances proliferation, cytokine production, cytotoxicity, and immune persistence following activation (Chester *et al.*, 2018). Historically, 4-1BB agonism has been viewed as one of the most promising immuno-oncology strategies due to its ability to amplify anti-tumor immune responses. However, early systemic 4-1BB agonists including urelumab encountered substantial hepatotoxicity and inflammatory toxicity due to widespread immune activation outside the tumor microenvironment.

ALG.APV-527 was specifically engineered to address these limitations through conditional immune activation. The molecule binds 5T4, an oncofetal antigen highly expressed across multiple solid tumors including non-small cell lung cancer, ovarian cancer, triple-negative breast cancer, and head and neck cancers, while simultaneously activating 4-1BB signaling only in the presence of tumor-associated 5T4 binding. This conditional activation strategy is intended to localize immune stimulation within the tumor microenvironment while reducing systemic immune toxicity.

Preclinical studies demonstrated tumor-directed T cell activation, enhanced cytokine production, and anti-tumor activity with potentially improved tolerability relative to earlier systemic 4-1BB agonists. A Phase 1 dose escalation trial was completed to evaluate up to six escalating dose levels (NCT05934539). The trial enrolled adult patients with multiple solid tumor types likely to express the 5T4 antigen. The compound was administered intravenously every two weeks. Results showed that no severe liver toxicity was observed and the drug exhibited linear pharmacokinetics. In regards to efficacy, 10/17 evaluable patients (59%) achieved stable disease (SD), and four of the patients had long-term SD of >10 cycles (~ 5 monhts) The longest SD duration was in a breast cancer patient who achieved SD and remained on study for >11 months with a transition to two higher dose levels.

APVO603 (4-1BB x OX40; Solid Tumors)
APVO603 is a preclinical dual-agonist bispecific generated using the ADAPTIR platform and designed to simultaneously target 4-1BB (CD137) and OX40 (CD134), both members of the TNF receptor superfamily. The therapeutic rationale is based on synergistic co-stimulation of immune effector cells, particularly activated T cells and NK cells, through simultaneous activation of complementary immune signaling pathways. OX40 signaling promotes T cell expansion, survival, memory formation, and cytokine production, while 4-1BB signaling enhances cytotoxic activity and immune persistence (Croft *et al.*,

2009). Combined activation of these pathways may potentially amplify anti-tumor immune responses while overcoming immunosuppressive tumor microenvironment signaling.

Importantly, APVO603 is not dependent on any single tumor-associated antigen and therefore may possess applicability across multiple solid tumor types. The molecule is currently advancing through IND-enabling studies.

APVO442 (PSMA-Directed Conditional T Cell Engager; Prostate Cancer)
APVO442 is a bispecific candidate generated using the ADAPTIR-FLEX platform and designed for later-stage and castration-resistant prostate cancer. The molecule targets prostate-specific membrane antigen (PSMA) expressed on prostate tumor cells while simultaneously activating T cells within the tumor microenvironment. Importantly, the construct was specifically engineered to avoid peripheral immune-cell activation and instead localize immune engagement within PSMA-expressing tumors.

According to the company, preclinical studies demonstrated preferential tumor localization while minimizing non-specific immune activation in circulation. In our view, this conditional activation strategy reflects one of the major themes emerging within next-generation solid tumor T cell engager development, namely improving therapeutic window through tumor-selective immune activation.

APVO711 (PD-L1 x CD40; Solid Tumors)
APVO711 is a bispecific checkpoint inhibitor generated using ADAPTIR-FLEX technology and designed to simultaneously target PD-L1 and CD40. The molecule integrates two clinically validated immuno-oncology mechanisms within a single construct: blockade of the PD-1/PD-L1 inhibitory checkpoint axis and CD40-mediated antigen-presenting cell activation.

The molecule was designed such that CD40 activation occurs primarily in the presence of PD-L1 engagement, thereby potentially reducing systemic immune toxicity associated with non-selective CD40 agonism. CD40 signaling enhances dendritic-cell maturation, antigen presentation, and T cell priming, while PD-L1 blockade restores anti-tumor T cell activity (Vonderheide, 2020). In our view, APVO711 represents one of the more mechanistically sophisticated assets within the company's pipeline and highlights the flexibility of the ADAPTIR-FLEX architecture for constructing multifunctional immune therapies.

APVO455 (Nectin-4 x CD3; Solid Tumors)
APVO455 is a preclinical Nectin-4 x CD3 bispecific T cell engager designed for solid tumors including bladder cancer, breast cancer, non-small cell lung cancer, and head and neck cancer, all of which frequently overexpress Nectin-4. Nectin-4 has emerged as an attractive oncology target following the clinical success of the Nectin-4-directed ADC enfortumab vedotin in urothelial carcinoma.

Unlike several competing conditional T cell engager approaches that rely on acidic tumor microenvironments or activated T cell states, APVO455 was specifically engineered to avoid peripheral T-cell activation unless Nectin-4-positive tumor cells are present. This strategy may potentially support broader therapeutic window optimization and reduce systemic immune toxicity while preserving robust anti-tumor cytotoxicity.

APVO451 (Nectin-4 x CD40 x CD3 Trispecific; Solid Tumors)
APVO451 is a trispecific immunotherapy candidate generated using ADAPTIR-FLEX technology and designed to simultaneously target Nectin-4, CD40, and CD3. The molecule incorporates dual mechanistic strategies intended to overcome immunosuppressive signaling within the solid tumor microenvironment. CD40 engagement promotes antigen-presenting cell maturation and cytokine production, thereby enhancing T cell priming, while CD3 engagement redirects cytotoxic T cells directly toward Nectin-4-expressing tumor cells. According to the company, early preclinical studies demonstrated potent anti-tumor activity even in the presence of suppressive tumor microenvironment conditions including PD-L1 expression and immunosuppressive myeloid-cell populations.

APVO452 (PSMA x CD40 x CD3 Trispecific; Prostate Cancer)
APVO452 utilizes a trispecific ADAPTIR-FLEX architecture targeting PSMA, CD40, and CD3 and is being developed for prostate cancer. Similar to APVO451, the molecule integrates simultaneous antigen-presenting cell activation and T cell redirection within a single therapeutic construct. Preclinical studies reportedly demonstrated selective killing of PSMA-expressing tumor cells while activating immune signaling only in the presence of tumor cells, potentially supporting improved safety characteristics.

In our view, APVO451 and APVO452 collectively highlight the increasing sophistication of the company's multispecific engineering strategy and demonstrate how ADAPTIR-FLEX may support development of highly integrated immunotherapy approaches combining tumor targeting, co-stimulation, checkpoint modulation, and T cell engagement within single therapeutic molecules.

Expansion into Radiopharmaceutical Development Through Niowave Collaboration

In May 2026, Aptevo Therapeutics announced a strategic collaboration with Niowave, Inc. focused on development of radiopharmaceutical therapeutics, representing an important continuation of Aptevo's work with an emerging treatment paradigm. Importantly, the agreement also included a strategic equity investment by Niowave into Aptevo, further aligning the interests of both organizations and providing external validation of Aptevo's underlying protein engineering capabilities.

We believe the collaboration is strategically significant for several reasons. First, it broadens the potential applicability of the ADAPTIR and ADAPTIR-FLEX platforms beyond T cell engagers and immune co-stimulatory biologics into adjacent targeted therapeutic modalities. Second, it positions the company to potentially participate in two of the fastest-growing sectors within oncology therapeutics: radiopharmaceuticals and next-generation targeted conjugates.

Under the collaboration, Aptevo and Niowave intend to explore use of Aptevo's antibody engineering capabilities together with Niowave's radioisotope production expertise to potentially develop targeted radiopharmaceutical therapeutics. Niowave possesses specialized infrastructure and technical expertise involving superconducting electron accelerator technology and medical isotope production, areas that have become increasingly important given ongoing supply-chain constraints surrounding therapeutic radioisotopes. In our view, access to isotope manufacturing capability may represent an increasingly valuable strategic differentiator as the radiopharmaceutical sector continues expanding.

Importantly, the collaboration appears highly complementary to Aptevo's broader platform strategy. Several of the company's existing tumor-targeting antibodies and multispecific constructs may theoretically be adaptable for conjugation-based or radioligand-based therapeutic applications. For example, highly tumor-selective binding domains derived from ADAPTIR-FLEX constructs could potentially support targeted payload delivery strategies while leveraging the company's existing expertise in conditional immune activation and tumor-localized targeting.

While the collaboration remains early and largely strategic in nature, Aptevo did disclose that it would initially contribute assets directly targeting Nectin-4, a clinically validated cancer target that is expressed on a broad range of solid tumors, while Niowave would provide radioisotopes, including Actinium-225. Thus, the two companies have a practical first program to build from against an established target. In addition, this collaboration reinforces management's broader strategic objective of positioning ADAPTIR and ADAPTIR-FLEX as versatile modular protein engineering systems applicable across multiple next-generation oncology therapeutic modalities.

From a competitive positioning standpoint, the move into radiopharmaceuticals may also help diversify the company beyond the increasingly crowded T cell engager field. While bispecific antibodies remain an important area of oncology innovation, investor enthusiasm has increasingly expanded toward targeted radioligand therapies and next-generation conjugate systems given their differentiated mechanisms and growing commercial validation.

Intellectual Property Position

Aptevo's ADAPTIR and ADAPTIR-FLEX platforms are protected through a combination of patents and trade secrets. The company owns all the intellectual property that covers each of those platforms, with the exception of licenses to certain third-party research tools that are used in conjunction with the ADAPTIR platform such as cell lines, vectors, expression systems, and transgenic rodents. Patents for ADAPTIR are issued in the U.S., Australia, Canada, Hong Kong, Israel, Japan, Mexico, New Zealand, Russia, Singapore, South Africa, and South Korea. There is also a pending application in Brazil. ADAPTIR-FLEX is covered by patent application under the Patent Cooperation Treaty (PCT) that was filed in 2021 and nationalized in 2023 in the U.S., Australia, Brazil, Canada, China, Europe, Israel, Japan, Mexico, New Zealand, Singapore, and South Korea.

Mipletamig is covered by a patent family in the U.S., Australia, Brazil, Canada, China, Colombia, Eurasia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Macau, Malaysia, Mexico, New Zealand, Philippines, Singapore, South Africa, South Korea, Ukraine, and Vietnam. Patents for ALG.APV-527, which are co-owned with Alligator Biosciences AB, corresponding to PCT application PCT/EP2018/069850 cover the ALG.APV-527 product candidate. Aptevo and Alligator also co-own U.S. patent 10,239,949, which relates to molecules that specifically bind to 5T4 and/or 4-1BB, and U.S. patent 11,312,786, which relates to 4-1BB binding domain. Alligator also owns a patent family corresponding to PCT application PCT/EP2017/059656, which also covers ALG.APV-527. Aptevo has an exclusive license from Alligator to this patent family for the development of ALG-APV-527.

Aptevo also owns pending patent applications for APVO442, APVO603, APVO711, APVO451, APVO452, and APVO455 preclinical candidates.

Financials and Capital Structure

In May 2026, Aptevo announced financial results for the first quarter of 2026. As expected, the company did not report any revenues for the period ending March 31, 2026. R&D expenses in the first quarter of 2026 were $3.9 million compared to $3.6 million in the first quarter of 2025. The increase was primarily due to increased mipletamig and employee costs. G&A expenses in each of the first quarters of 2026 and 2025 were $2.8 million.

Aptevo exited the first quarter of 2026 with approximately $14.5 million in cash and cash equivalents. During the quarter, the company entered into a $60 million Standby Equity Purchase Agreement (SEPA) with Yorkville Advisors Global, LP. The facility allows Aptevo to raise funds incrementally under market-based conditions by giving the company the right, but not the obligation, to sell shares to Yorkville at its discretion. During the first quarter of 2026, Aptevo raised approximately $0.9 million under the company's SEPA with Yorkville. Considering the SEPA and the company's current cash position, we estimate Aptevo's cash runway extends into 2029. As of May 13, 2026, Aptevo had approximately 1.3 million shares outstanding and, when considering restricted stock units and warrants, a fully diluted share count of 1.9 million.

Risks to Consider

In addition to the risk factors listed below, investors are encouraged to read the company's most recent 10-K filing that discusses additional risk factors.

Development Risk: Aptevo is a clinical-stage biotechnology company with no approved commercial products and, therefore, remains heavily dependent on the successful clinical advancement of its pipeline candidates, particularly mipletamig. Although the company has generated encouraging early clinical data with mipletamig in frontline AML, ther current dataset remains relatively small, immature, and early-stage. Many oncology programs that initially demonstrated promising Phase 1 and Phase 2 data have ultimately failed to reproduce those findings in larger randomized studies. In addition, while the absence of CRS reported to date may represent an important differentiating feature of mipletamig, it remains possible that

immune-related toxicities could emerge as additional patients are enrolled at higher dose levels or with longer duration of therapy. The company's broader pipeline remains predominantly preclinical and those assets remain subject to the substantial risk inherent to early-stage immunotherapy development.

Clinical and Regulatory Risk: Clinical development timelines within oncology remain inherently uncertain and subject to significant regulatory risk. Although the FDA has increasingly supported accelerated development pathways for therapies addressing high unmet medical need in AML, there can be no assurance that Aptevo's ongoing or future studies will ultimately support regulatory approval. In addition, evolving regulatory standards surrounding MRD, surrogate endpoints, and accelerated approval pathways may affect future development strategy. While MRD negativity is increasingly recognized as an important prognostic marker in AML, regulatory acceptance of MRD as a validated surrogate endpoint remains an evolving area. The company also faces potential manufacturing and chemistry, manufacturing, and controls (CMC) risks associated with increasingly complex multispecific biologic architecture. Production of stable bispecific and trispecific antibodies remains technically challenging, and manufacturing scalability issues could potentially emerge as programs advance into later-stage development.

Commercial Risk: Even if mipletamig or other pipeline candidates ultimately achieve regulatory approval, substantial commercial risk would remain. The AML treatment landscape has become increasingly competitive following multiple recent approvals involving targeted therapies, BCL-2 inhibitors, FLT3 inhibitors, IDH inhibitors, menin inhibitors, antibody-drug conjugates, and emerging immunotherapies. Large pharmaceutical companies with substantially greater financial resources, commercial infrastructure, and development capabilities are actively pursuing additional AML therapies across multiple mechanistic classes. Venetoclax-based regimens are already deeply integrated into frontline AML treatment paradigms, and physicians may be reluctant to add additional immunotherapy agents unless substantial improvements in durability, survival, or tolerability are clearly demonstrated. Commercial adoption may therefore depend heavily on the magnitude of incremental clinical benefit ultimately demonstrated in larger studies.

Strategic and Execution Risk: Execution risk remains significant for small clinical-stage biotechnology companies operating multiple pipeline programs simultaneously. Aptevo must successfully manage clinical operations, manufacturing development, regulatory interactions, intellectual property strategy, business development initiatives, and capital allocation decisions while operating with comparatively limited financial and organizational resources relative to larger competitors. The company's long-term success may also depend on its ability to establish strategic partnerships capable of supporting later-stage development and commercialization activities. There can be no assurance that future partnership opportunities will emerge on favorable terms, if at all. Finally, key-person dependency remains an important consideration. Loss of senior scientific leadership, clinical development personnel, or platform engineering expertise could negatively affect execution timelines and broader corporate strategy.

MANAGEMENT PROFILES

Jeff Lamothe, President and Chief Executive Officer

Jeff Lamothe is President and Chief Executive Officer of Aptevo Therapeutics and a member of the Board of Directors. He leads the development and execution of corporate strategy as Aptevo advances differentiated immuno-oncology therapies built on its proprietary ADAPTIR™ and ADAPTIR-FLEX™ platforms. Mr. Lamothe brings deep executive leadership experience to the role, including more than 20 years serving in C-suite positions as Chief Executive Officer, Chief Operating Officer, and Chief Financial Officer across multiple industries. As a founding member of Aptevo's leadership team, Mr. Lamothe progressed from Chief Financial Officer to Chief Operating Officer and now Chief Executive Officer. As COO, he oversaw Clinical, Research and Development, Quality, Manufacturing, and Operations, advancing multiple programs in parallel. Earlier, as CFO, he led Finance, Business Development, Investor Relations, and Information Technology, helping to establish the strategic and financial framework that supported the company's growth. Prior to joining Aptevo, he served as Vice President Finance, Biosciences Division at Emergent BioSolutions following its acquisition of Cangene Corporation, where he was Chief Financial Officer.

Daphne Taylor, Senior Vice President and Chief Financial Officer

Daphne Taylor is Senior Vice President and Chief Financial Officer of Aptevo Therapeutics, providing strategic direction to financial operations including audit, tax, accounting, purchasing, treasury, forecasting, budgeting, risk management, and ensuring regulatory compliance. She also oversees Investor Relations, and Information Technology, aligning performance with long-term growth. Before joining Aptevo, Ms. Taylor served as Chief Financial Officer at BioLife Solutions and held senior finance roles at Cardiac Science Corporation, LookSmart, SpeedTrak, Core-Mark International, and Pacific Telesis. She began her career at Coopers & Lybrand in San Francisco. Ms. Taylor serves as a leader at Executive Women in Bio (Seattle chapter), holds a B.A. from Sonoma State University, and is Certified Public Accountant in Washington and California.

Dirk Huebner, M.D., Senior Vice President and Chief Medical Officer

Dr. Dirk Huebner is Chief Medical Officer and brings three decades of academic and industry-based clinical drug development experience across the biotech and pharmaceutical sectors. He leads Aptevo's clinical strategy and execution from early-stage studies through late-stage development. Previously, Dr. Huebner served as Chief Medical Officer and Senior Medical Advisor at Mersana (2018–2021), where he built the clinical development department and oversaw the ADC pipeline. Earlier, as Vice President and Head of Development at Boston Biomedical, he assembled a robust clinical team and led multiple early-stage programs, including the napabucasin Phase 3 program. At Millennium/Takeda Oncology, he was Executive Medical Director and global clinical lead for ADCETRIS® (brentuximab vedotin), guiding its European regulatory approval and subsequent registration-enabling studies. He also served as clinical lead for clofarabine in acute myeloid leukemia at Genzyme and held roles of increasing responsibility at Roche and Bristol-Myers Squibb. Dr. Huebner holds an M.D. from Freie Universität Berlin and completed his medical residency at the Department of Urology, University Hospital Eppendorf (Hamburg).

Mary J. Janatpour, PhD – Senior Vice President and Chief Scientific Officer

Dr. Mary J. Janatpour leads Aptevo's research and development strategy, with responsibility for advancing preclinical assets developed from the Company's proprietary ADAPTIR™ and ADAPTIR-FLEX™ platforms and building a differentiated pipeline of cancer therapeutics. She brings more than 35 years of biomedical research experience, including more than 25 years helping biotechnology and pharmaceutical companies translate novel platforms into value-building oncology pipelines. Dr. Janatpour has held senior scientific leadership roles across established biopharmaceutical organizations and emerging biotechnology companies, giving her a rare combination of large-company oncology research discipline and hands-on experience building innovative programs in fast-moving development environments. Earlier in her career, she held leadership positions at the Novartis Institutes for Biomedical Research, Schering-Plough Biopharma and Chiron, where her work focused on oncology biologics target

identification and validation. The latter half of her career has been focused on immuno-oncology. At Dynavax she oversaw an immuno-oncology clinical program and research to inform rational combinations. Most recently she served as CSO at biotechnology companies developing novel platform-based approaches in immuno-oncology that included targeted in situ delivery of gene editors, as well as a bacterial vector platform. She also serves on the Board of Directors of Active Motif, is a scientific advisor to Mithrl and Cypre, and has served as an independent consultant to immuno-oncology start-ups. Dr. Janatpour holds a BA in Molecular Biology from the University of California, Berkeley, and a PhD in Biomedical Science from the University of California, San Francisco. She completed her postdoctoral training in Immunology at the DNAX Research Institute in Palo Alto, California.

SoYoung Kwon, Senior Vice President and General Counsel, BD and Corporate Affairs

SoYoung Kwon is Senior Vice President and General Counsel of Aptevo Therapeutics. She leads Legal, Compliance, Business Development, Human Resources and Facilities, overseeing corporate governance, securities, compliance, contractual and intellectual property matters, talent and organizational development, facilities and safety. Ms. Kwon brings more than 30 years of legal and business leadership across regulated and innovation-driven industries. Prior to Aptevo, Ms. Kwon served as Global Senior Vice President, General Counsel, and Corporate Secretary and business development leader at AGC Biologics, a global contract development and manufacturing organization with facilities in the U.S., Europe, and Asia. She also served as Vice President, General Counsel, and Corporate Secretary and Head of Human Resources at Onvia, Inc.; Senior Counsel at Safeco Corporation; and Corporate Associate at Graham & Dunn PC. Her experience spans insurance, high-tech, biologics, and cell and gene therapy. Ms. Kwon is a Trustee of the Seattle Art Museum, where she serves as a member of the Executive Committee. She also serves as President of the Washington Scholarship Foundation.

Miriam Weber Miller, Vice President, Investor Relations and Corporate Communications

Miriam Weber Miller is Vice President of Investor Relations and Corporate Communications at Aptevo Therapeutics. She leads investor engagement and enterprise communications across investors, employees, partners, media, and the Board of Directors, shaping corporate narrative and market positioning. Ms. Miller brings more than 20 years of experience in investor relations, public relations, and corporate communications within healthcare. She has worked with early-stage biotech and publicly traded pharmaceutical organizations, with deep expertise in investor strategy, clinical data positioning, and corporate storytelling in high-visibility environments. Prior to Aptevo, she held senior leadership positions at Tiberend Strategic Advisors and Finn Partners and helped build the life sciences communications practice at Porter Novelli, leading programs around IPOs and strategic transactions and managing high-performing teams. Ms. Miller holds a M.B.A. (Finance) from Fordham University and a B.A. (Journalism) from Rowan University.

VALUATION

We are initiating coverage of Aptevo Therapeutics Inc. (APVO) with a valuation of $30.00. Aptevo is a clinical-stage biopharmaceutical company focused on the development of multispecific immunotherapies designed to engage and modulate the immune system for the treatment of cancer. The company's therapeutic approach centers around its proprietary ADAPTIR and ADAPTIR-FLEX platform technologies, which are capable of generating mono-, bi-, and trispecific immune-engaging proteins with customizable structural and functional properties. Importantly, both platforms have already generated multiple clinical-stage and preclinical assets spanning both hematologic malignancies and solid tumors, with mipletamig and ALG.APV-527 emerging as the company's lead development products.

Mipletamig

The company's lead asset, mipletamig, is a CD123 x CD3 bispecific T cell engager generated using the company's ADAPTIR platform and was specifically engineered to redirect endogenous cytotoxic T cells toward leukemic blasts and leukemic stem cells expressing CD123. Unlike many earlier-generation T cell engagers that utilized highly potent CD3-binding domains associated with substantial cytokine release syndrome (CRS), mipletamig incorporates Aptevo's proprietary CRIS-7-derived CD3 binding domain, which was designed to preserve anti-leukemic activity while reducing excessive immune activation and inflammatory cytokine release.

Mipletamig has now been evaluated across multiple clinical studies, including early monotherapy dose-escalation trials, dose-expansion studies, and the ongoing Phase 1b/2 RAINIER frontline AML trial. Collectively, the molecule has been administered to more than 120 patients to date, providing a meaningful emerging safety database for a CD3-engaging therapy in AML. The ongoing RAINIER study is a Phase 1b/2, multi-center, open-label trial evaluating mipletamig in combination with venetoclax and azacitidine in newly diagnosed AML patients who are ineligible for intensive induction chemotherapy. The trial is designed as a dose-optimization study intended to identify the recommended Phase 2 dose (RP2D) while simultaneously generating preliminary efficacy and safety data across escalating dose cohorts.

In May 2026, Aptevo released the most recent RAINIER update, which included data from 31 evaluable frontline AML patients treated through Cohort 5, including 27 patients enrolled in RAINIER and four additional patients from the prior dose-expansion study. The results were highly encouraging and, in our view, represent the strongest dataset generated to date for the program. Across the evaluable population, mipletamig in combination with venetoclax and azacitidine produced an 87% clinical benefit rate, defined as complete remission (CR), complete remission with incomplete hematologic recovery (CRi), or partial remission (PR). Most notably, 81% of patients achieved CR/CRi, while 65% achieved complete remission.

Perhaps the most differentiating aspect of the RAINIER dataset to date is the apparent safety profile. Importantly, no CRS has been reported in frontline AML patients treated through Cohort 5 of the RAINIER study. This observation is potentially highly significant within the broader context of T cell engager development. In addition, the absence of CRS observed thus far may support management's thesis that the CRIS-7-derived CD3 binding domain meaningfully modulates immune activation while preserving anti-tumor cytotoxicity.

ALG.APV-527

ALG.APV-527 represents Aptevo's second clinical-stage asset and was developed in collaboration with Alligator Bioscience using the ADAPTIR-FLEX platform. The molecule is a tumor-directed 4-1BB agonistic bispecific antibody targeting both 4-1BB (CD137) and 5T4. 4-1BB is a potent co-stimulatory

receptor expressed on activated T cells and NK cells that enhances proliferation, cytokine production, cytotoxicity, and immune persistence following activation. Historically, 4-1BB agonism has been viewed as one of the most promising immuno-oncology strategies due to its ability to amplify anti-tumor immune responses. However, early systemic 4-1BB agonists including urelumab encountered substantial hepatotoxicity and inflammatory toxicity due to widespread immune activation outside the tumor microenvironment.

ALG.APV-527 was specifically engineered to address these limitations through conditional immune activation. The molecule binds 5T4, an oncofetal antigen highly expressed across multiple solid tumors including non-small cell lung cancer, ovarian cancer, triple-negative breast cancer, and head and neck cancers, while simultaneously activating 4-1BB signaling only in the presence of tumor-associated 5T4 binding. This conditional activation strategy is intended to localize immune stimulation within the tumor microenvironment while reducing systemic immune toxicity.

Preclinical studies demonstrated tumor-directed T cell activation, enhanced cytokine production, and anti-tumor activity with potentially improved tolerability relative to earlier systemic 4-1BB agonists. A Phase 1 dose escalation trial was completed to evaluate up to six escalating dose levels. The trial enrolled adult patients with multiple solid tumor types likely to express the 5T4 antigen. The compound was administered intravenously every two weeks. Results showed that no severe liver toxicity was observed and the drug exhibited linear pharmacokinetics. In regards to efficacy, 10/17 evaluable patients (59%) achieved stable disease (SD), and four of the patients had long-term SD of >10 cycles (~ 5 monhts) The longest SD duration was in a breast cancer patient who achieved SD and remained on study for >11 months with a transition to two higher dose levels.

Valuation

We value Aptevo using a probability-adjusted discounted cash flow model that takes into account revenues from mipletamig and ALG-AVP-527 along with a modest contribution from the underlying ADAPTIR and ADAPTIR-FLEX platform technologies and the Niowave collaboration. Given the early stage of development of the remainder of the pipeline, including APVO603, APVO442, APVO711, APVO451, APVO452, and APVO455, we do not currently assign explicit valuation to these programs.

For mipletamig, we estimate there are approximately 25,000 newly diagnosed AML patients annually in the U.S. and major European markets that fall within the addressable population targeted by mipletamig. Given the encouraging remission rates reported from the ongoing RAINIER study, including high rates of MRD-negative remission and the absence of CRS reported to date, we believe mipletamig has the potential to capture meaningful market share if future studies continue to demonstrate a differentiated balance of equity and tolerability.

We assume peak global market penetration of approximately 30% within the frontline unfit AML population and annual net pricing of approximately $125,000 per patient in the U.S. and $65,000 in the E.U., which results in projected peak revenues of approximately $1.0 billion seven years after approval in 2030. Using a probability of success of 33% and a 13% discount rate leads to a net present value for mipletamig of approximately $258 million.

For ALG.APV-527, even though the asset is much earlier in development than mipletamig we believe it contributes meaningful strategic value as it serves not only as an individual therapeutic program but also as a clinical validation opportunity for the broader ADAPTIR-FLEX platform. Given the large potential commercial opportunities across multiple solid tumor indications we model peak annual revenues of approximately $1.5 billion seven years after approval in 2032. Using a probability of success of 10% and a 13% discount rate leads to a net present value for ALG.APV-527 of $30 million.

In addition to the clinical stage assets, we believe the ADAPTIR and ADAPTIR-FLEX platforms and the Niowave collaboration possess independent strategic value based on the existence of two clinical stage molecules, a broad intellectual property portfolio, multiple partnered development programs, and the

potential for future licensing, collaboration, and business development opportunities. While we do not currently assign significant value to the company's preclinical assets, we assign a value of $50 million to the underlying platform technologies and Niowave partnership opportunity.

Combining the net present value for mipletamig, ALG.AVP-527, and the platform/partnering opportunities along with the current cash position and potential cash from warrant exercises leads to a net present value for Aptevo of $361 million. Dividing by the fully diluted share count (approximately 1.9 million) plus an additional 10 million shares to account for additional financings leads to a valuation of $30 per share.

PROJECTED FINANCIALS

Aptevo Therapeutics Inc.	2025 A	Q1 A	Q2 E	Q3 E	Q4 E	2026 E	2027 E	2028 E
Mipletamig	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
ALG.APV-527	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
License and other revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
Cost of revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Research & development	$14.5	$3.9	$4.0	$4.0	$4.1	$16.0	$18.0	$20.0
General & administrative	$11.8	$2.9	$3.0	$3.0	$3.1	$12.0	$12.5	$13.0
Operating Income	($26.3)	($6.8)	($7.0)	($7.0)	($7.2)	($28.0)	($30.5)	($33.0)
Non-Operating Expenses (Net)	$0.3	$0.1	$0.1	$0.1	$0.1	$0.4	$0.4	$0.4
Pre-Tax Income	($26.0)	($6.7)	($6.9)	($6.9)	($7.1)	($27.6)	($30.1)	($32.6)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Income	**($26.0)**	**($6.7)**	**($6.9)**	**($6.9)**	**($7.1)**	**($27.6)**	**($30.1)**	**($32.6)**
Dividend attributable to down round feature of warrants	$1.6	$0.1	$0.1	$0.1	$0.1	$0.4	$0.5	$0.5
Net Income Attributable to Common Shareholders	**($27.5)**	($6.8)	($7.0)	($7.0)	($7.2)	($28.0)	($30.6)	($33.1)
Reported EPS	**($87.27)**	**($6.41)**	**($5.83)**	**($5.38)**	**($5.14)**	**($22.57)**	**($2.78)**	**($2.36)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	0.3	1.1	1.2	1.3	1.4	1.2	11.0	14.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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