Letter to Aptevo Shareholders

To My Fellow Shareholders,

As the annual meeting approaches, I want to take this time to reflect on where we are as a Company and where we expect to be at this time next year.

Over the last twelve months we focused heavily on advancing our clinical programs. Some of this was visible. For example, we released strong durability of remission data (DoR) from our APVO436 Phase 1b dose expansion trial. This data included one patient who responded to treatment for eight cycles, the maximum allowed on protocol and three patients who advanced to transplant from study. This is the best possible outcome for an AML patient and the only possibility for a cure. The DoR data, together with already reported safety and efficacy data that significantly out-performs benchmarks from literature, supports our belief that APVO436 has significant potential to add to the standard-of-care and improve outcomes for AML patients with limited existing treatment options.

Some of our work on APVO436 was not so visible. Upon the conclusion of the Phase 1b trial we worked closely with the FDA to determine the most effective next steps to further derisk and differentiate our therapy in the AML treatment space. While this work took time, this time was well spent and we now have a go forward strategy.

We concluded that a Phase 1b/2 trial in frontline AML patients, conducted in two parts, was the best next step. The first part will be a Phase 1b dose optimization, open label multi-cohort study in combination with standard of care venetoclax + azacitidine in venetoclax naïve patients. We plan to initiate this part late in the second quarter. The trial will evaluate safety and efficacy independently and in relation to dose. This is to ensure that we identify the point at which APVO436 provides the most clinical benefit with the lowest risk of side effects, in particular, Cytokine Release Syndrome (CRS), a serious and sometimes treatment-limiting adverse event.

Immune therapy as a category is characterized by high rates of CRS but APVO436 was designed to reduce cytokine release and reduce incidence of the syndrome. The great news is that APVO436 is performing in the clinic as we designed it and as it performed in the lab. In total, 90 patients have been treated with APVO436 and only 27% experienced CRS. This is approximately one-third of the benchmark comparisons found in literature. Upon conclusion of the dose optimization study, we plan to initiate a Phase 2 trial.

We are really excited about moving APVO436 forward. The data indicate that the compound holds significant promise for patients fighting AML. It also demonstrates the power of our first proprietary platform, ADAPTIR, to produce a powerful bispecific anti-cancer agent with a safety profile that reduces the risk of serious adverse events.

ALG.APV-527, our 4-1BB x 5T4 co-stimulatory molecule is also in the clinic and being evaluated for the treatment of multiple solid tumor types likely to express 5T4. We initiated a Phase 1 open label, multi-center, multi-cohort dose escalation trial last year. As of this communication the trial is more than 50% enrolled and dosing in cohort 5 (of 6) has been initiated.

We released early data from this trial in March. Excitingly, ALG.APV-527, like APVO436, is built with purpose: to overcome the safety challenges of first-generation 4-1BB agonists by requiring the presence of 5T4 for activation and promote a targeted response that limits systemic exposure.

A highlight of our data is a breast cancer patient who entered the trial and improved from progressive disease to long-lasting stable disease (SD) while on therapy. The patient has remained on study for more than nine months and been successfully transitioned to a higher dose level, which may allow for increased clinical benefit. This is an uncommon occurrence in early solid tumor trials and even more uncommon because the patient entered the trial with progressive disease.

A second heavily pretreated breast cancer patient who was progressing prior to enrolling in the trial also sustained long lasting stable disease and remained on study drug for seven months. Additionally, our analysis demonstrated measurable level of drug in circulation (pharmacokinetic) and reproducible elevation of serum pharmacodynamic markers with dosing, suggesting the drug is biologically active. Biological activity is a critical point of analysis in early stage clinical trials.

It's important to remember that these are early days for this trial and for the development of ALG.APV-527 but outcomes such as those we have seen with the two breast cancer patients, although anecdotal, are exciting and reinforce our belief that this solid-tumor directed anti-cancer agent has great potential, answering the question “does it show up in the body in therapeutically meaningful quantities?”

While our primary focus was, and continues to be, on our candidates in the clinic, we continue to progress the preclinical pipeline. Of particular interest is our newest pre-clinical candidate, APVO711. This is a dual mechanism checkpoint inhibitor with added functionality that is also built for precision tumor targeting that limits systemic exposure. We recently released information about our key learnings for this molecule, including:

- APVO711 imparts beneficial attributes to both antigen presenting cells and T cells that boost the immune response targeted at controlling tumor cells
- Experiments in cultured cells have confirmed that APVO711 enhances tumor cell killing by T cells
- *In vivo* studies have confirmed that APVO711 reduces the size of PD-L1-expressing tumors

The year was not without challenges. Microcap biotechnology companies continue to have difficulty accessing capital and Aptevo was no exception. We made difficult choices to accept capital under less than ideal terms. We did so to secure critical funding that allows us to continue our work. We firmly believe our therapeutics have great potential to positively impact the cancer treatment paradigm in AML and across a range of solid tumors. We believe the growing body of data released over the last two years demonstrates that potential and more recently released data further supports the story. So, while we raised money in a very difficult market, we did raise money and we continue to see results that demonstrate the potential of our assets for cancer patients.

The critical points to our story are that we are building differentiated assets specifically designed for safety, precision tumor killing and combinability with standard of care. This last point is particularly important in cancer treatment today, where combination therapies dominate the standard of care across most cancer types.

In the year ahead, you can expect to hear from us across multiple fronts. In our APVO436 program we plan to initiate the dose optimization trial this quarter and will report interim results by the end of the year. The ALG.APV-527 Phase 1b dose escalation trial in solid tumors will be concluded by the end of the year and we plan to announce preliminary results. We will also initiate planning for the dose expansion part of the ALG.APV-527 trial, which will potentially be in combination therapy. We will continue to advance our preclinical pipeline, with emphasis on our unique and highly targeted molecule, APVO711, which demonstrates the flexibility of our platform to evolve therapeutics relevant to the market.

I'll close here with a quote from Abraham Lincoln who said, "*The best way to predict your future is to create it*." Thank you for helping us create a world in which patients with cancer have the potential to live longer, live stronger and live well.

Marvin White
President and CEO
Aptevo Therapeutics