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Restated Rules

- **Budget Discipline:** No new capital beyond the current portfolio value ($81.80). All trades must use existing cash or proceeds from sales – we cannot exceed the available cash. We will track cash precisely after each transaction to ensure we stay within budget.
- **Execution Limits:** Trades are **full shares only** – no fractional shares. We cannot use options, short selling, leverage, margin, or any derivatives. All positions are **long-only** stock positions. We prefer to use limit orders (Day orders unless specified otherwise) for execution, aiming to get filled near current market prices.
- **Universe Constraints:** We focus on U.S.-listed micro-cap stocks with **market capitalizations under $300M** at time of purchase. We will verify the market cap of any new buy using the latest price and share count. (If an existing holding later exceeds $300M, we can hold or sell it, but not add more.)
- **Liquidity and Slippage:** We must respect liquidity – only trading names with sufficient average volume so our orders are a small fraction of daily volume. We avoid names with very wide bid/ask spreads to minimize slippage.
- **Risk Controls:** We maintain stop-loss orders on all long positions, as provided or appropriately adjusted. We will **immediately flag and address** any breaches of risk constraints (e.g. oversize positions, missing stop-loss, or forbidden assets). No single position should dominate the portfolio in a way that violates prudent risk management, and overall portfolio beta and volatility should be monitored.
- **Cadence and Flexibility:** This is the weekly deep research window (Week 16 of the 6-month experiment). We have **full discretion** to adjust the portfolio – including adding new stocks, trimming, exiting, or increasing positions – in pursuit of better risk-adjusted returns. All moves will be backed by deep research and a clear catalyst-driven rationale. We will implement **position sizing and stop levels** consistent with the stated rules to optimize the portfolio's return for the remaining weeks of the experiment.

Research Scope

For this week's analysis, I conducted extensive research on both our **current holdings** and potential **new candidates**, focusing on recent developments, upcoming catalysts, and market conditions: - **Current Holdings Research:** Reviewed the latest news and performance of each holding. For Spero Therapeutics (SPRO), I confirmed GSK's plan to file the NDA for tebipenem HBr in **2H 2025** (likely imminently) [1], which aligns with our thesis that SPRO is approaching a regulatory inflection point. For OKYO Pharma (OKYO), I reviewed its successful Phase 2 trial in neuropathic corneal pain (NCP) – the topline data in July showed 75% of patients had >80% pain reduction [2]. However, the next step is a larger 100-patient trial with data not expected until 2026 [3] [4], meaning no near-term catalyst. For Tiziana Life Sciences (TLSA), I surveyed their recent progress with intranasal foralumab. Notably, the stock is up over **+227% YTD** as of August [5] on multiple positive developments, including Phase 2 trials starting in progressive MS and **new indications** (e.g. the first patient was dosed in a trial for **multiple system atrophy** in August [6]). Tiziana also received a U.S. DoD grant in September to study foralumab in spinal cord injury [7] – a vote of confidence and a source of non-dilutive funding. These updates confirm TLSA's momentum and broadened pipeline, though major clinical readouts will come later.
- **Catalyst Scan for New Opportunities:** I scoured FDA calendars and biotech news for micro-cap stocks

with **significant Q4 2025 catalysts**. A key finding was **Milestone Pharmaceuticals (MIST)** – a ~$200M market-cap biotech with a **December 13, 2025 PDUFA date** for its drug etripamil (nasal spray "CARDAMYST™") in paroxysmal supraventricular tachycardia [8] [9]. This PDUFA is a high-impact binary event in our time frame. Research showed MIST received a Complete Response Letter (CRL) earlier in March due to manufacturing issues, but has since resolved them and the FDA has accepted the resubmission [10]. Analysts note the FDA had "no concerns regarding clinical data" in the CRL [11], suggesting a favorable setup for approval. The risk/reward on MIST appears very attractive: at ~$2/share it trades at ~$200M market cap, whereas approval could re-rate it toward a ~$750M+ valuation according to estimates [9] (i.e. a multi-bagger potential). I verified liquidity (~1.3M shares/day) and confirmed market cap ~ $200M [9] – well below our $300M limit. This makes MIST a prime candidate.
- I also considered a couple of other catalysts: **IO Biotech (IOBT)** has a Phase 3 cancer vaccine data update (oral presentation at ESMO 2025) after its melanoma trial *just missed* statistical significance in August (p=0.056) [12]. While the data showed meaningful PFS improvement (19.4 vs 11.0 months) and some subgroup significance [13] [14], the regulatory path is riskier. Given our limited time, I decided not to initiate IOBT now, but I will monitor it. Another was **Aldeyra (ALDX)**, which we know has a December 16 PDUFA for dry eye drug Reproxalap. However, Aldeyra's market cap is currently about **$319M** [15] – slightly above our micro-cap cutoff, so we cannot re-enter it. Thus, MIST emerged as the standout new trade.
- All information was cross-verified using company releases, credible news (FierceBiotech, GlobeNewswire, etc.), and market data. I ensured each potential name meets our criteria (market cap, liquidity, catalyst timeline). The research gives us confidence in the actions we plan to take, focusing on high-conviction catalysts while trimming exposure to names with less immediate upside.

(Sources: Company press releases and financial data for SPRO, OKYO, TLSA; Nasdaq/InvestingNews Network list of top 2025 small-cap biotechs [16] [17]; AInvest analysis on MIST's December PDUFA [8] [9]; IO Biotech trial result release [12] [14].)

Current Portfolio Assessment

Overview: The portfolio currently has three micro-cap biotech positions. Below is an assessment of each holding, including its role in our strategy, entry details, cost basis, stop-loss, and current outlook:

- **SPRO (Spero Therapeutics)** – **Role:** Turnaround partnership play in antibiotics (lower-risk, steady grower). **Entry Date/Price:** Initiated Week 13 at $2.09 average. **Cost Basis:** $45.99 total ($2.090/share). **Current Stop:** $1.78 (in place, ~15% below cost). **Conviction:** High. **Status:** *Holding*. SPRO remains a core position due to its partnership with GSK on tebipenem HBr. Our thesis is playing out: the Phase 3 trial met its endpoint and was stopped early for efficacy [1], and GSK is on track to file the NDA by end of 2025 [1]. Spero's ~$125M market cap [18] does not yet reflect the high likelihood of FDA approval given GSK's backing and priority designations. The company is well-capitalized (runway into 2028 [19]), reducing dilution risk. We maintain a high conviction that SPRO will appreciate as the NDA filing and any related milestones (e.g. FDA acceptance news) come through. The stock has risen modestly (last ~$2.28) from our entry, but still trades cheaply relative to its potential first-in-class oral antibiotic. We will **continue to hold** SPRO, but plan to trim the position size to manage risk (it was over 60% of our portfolio) while still keeping a significant exposure. Stop-loss at $1.78 remains appropriate (just under recent support ~$1.80).

- **OKYO (OKYO Pharma)** – **Role:** Ophthalmic drug catalyst play (high risk/reward, but longer timeline). **Entry Date/Price:** Initiated Week 14 at $2.08. **Cost Basis:** $20.80 total ($2.080/share). **Current Stop:**

$1.75 (~15% below cost). **Conviction:** Moderate (reduced). **Status:** *Reviewing for Exit*. OKYO achieved a **fast-track** designation and positive Phase 2 results in neuropathic corneal pain (NCP) this summer [2] [20], which drove the stock to a YTD high of $3.17 in August [21]. However, with that catalyst now past, OKYO is transitioning into a development phase: the next trial (100-patient multi-center Phase 2b) is planned, with topline data not until 2026 [3] [4]. Near-term news flow may slow (aside from routine updates or partnership attempts). The stock has pulled back to ~$1.95. We are concerned about the lack of catalysts in our remaining 10-week window and the possibility of dilution to fund the larger trial (the company did receive a small $1.9M grant [21], but that won't fund a 100-patient study fully). Given these factors, our conviction has decreased. We plan to **exit OKYO** to free up capital for more immediate opportunities. We will close the position and remove the stop.

- **TLSA (Tiziana Life Sciences)** – **Role:** Innovative immunotherapy platform play (pipeline in neuro-immunology; medium-term catalysts, plus momentum). **Entry Date/Price:** Initiated Week 15 at $1.99. **Cost Basis:** $11.94 total ($1.990/share). **Current Stop:** $1.78 (~10% below cost). **Conviction:** Moderately High. **Status:** *Holding (Keep)*. Tiziana has been a star performer this year (up over +220% YTD) [5], and we bought in due to its promising intranasal foralumab (a unique fully human anti-CD3 mAb) for progressive MS, ALS, and other diseases. The company has continually delivered encouraging news: dosing has begun in a Phase 2a MS trial and a Phase 2a **MSA** trial (first patient dosed on Aug 14) [6], and exploratory use in Alzheimer's showed intriguing biomarker improvements [22]. In addition, Tiziana just secured a **DoD grant** to study spinal cord injury [7], highlighting the broad potential of its approach and providing non-dilutive funding. We view TLSA as a longer-term play, but its strong news flow and insider buying (executives and the Chairman bought shares this summer around $1.60–1.65 [23] [24]) add confidence. While major Phase 2 data readouts won't occur until 2024-2025, the stock could continue to climb on incremental milestones (trial progress, partnerships, etc.). We will **keep our TLSA position** at 6 shares (approximately 15% of the portfolio). The stop-loss at $1.78 is set just below recent support levels and the CEO's purchase price, which we believe is appropriate. We note that TLSA's market cap is ~$233M [25] (within limits) and it has no debt with a recent ~$3.5M raise in Sep 2025 to extend its cash runway [26]. Our conviction remains strong that TLSA's novel therapy could attract strategic interest or further rally as clinical progress continues. We'll maintain the position as a diversifier (autoimmune/neuro focus) in our catalyst-driven basket.

(Current holdings summary: After exiting OKYO, we will have SPRO (~42% of portfolio after trimming), TLSA (~15%), and a new position MIST ~43% – see below. All remaining holdings comply with the < $300M cap rule: SPRO ~$126M [18], TLSA ~$234M [25]. Each also has adequate liquidity, trading hundreds of thousands of shares per day, see Risk Checks.)

Candidate Set

After evaluating numerous small-cap biotech candidates, I narrowed the focus to a few that fit our catalyst and size criteria. Key candidates considered:

- **MIST – Milestone Pharmaceuticals** (NASDAQ:MIST): *Thesis:* High-probability FDA approval play. Milestone's intranasal etripamil (brand "Cardamyst") for paroxysmal supraventricular tachycardia has a **PDUFA on Dec 13, 2025**, which is the defining catalyst [8]. The drug addresses an unmet need (at-home PSVT treatment) and had no efficacy issues in its NDA – only CMC issues which have been resolved [10]. *Catalyst:* FDA approval decision (binary event). *Market Cap:* ~$200M [9] (micro-cap).

Liquidity: ~1–1.5M shares/day (ample [27]). *Notes:* A successful approval could re-rate MIST dramatically – analysts project **3-4x upside** ($750M+ valuation) if approved [9], with downside cushioned by prior RTW funding and the fact that the CRL was manufacturing-related, not clinical. This strong risk-reward and near-term catalyst make MIST our top pick for new addition.

- **IOBT – IO Biotech** (NASDAQ:IOBT): *Thesis:* Cancer immunotherapy (therapeutic vaccine) with a recent pivotal trial. Its Phase 3 in advanced melanoma (IO102-103 vaccine + Keytruda) showed **improved PFS** (19.4 vs 11.0 months) but narrowly missed stat. significance (p=0.056) [12]. The company plans to meet FDA to discuss a regulatory path given strong subgroup efficacy (PD-L1 negative patients had p=0.006) [28]. *Catalyst:* Potential **regulatory filing** or partnership news; ESMO late-breaker data presentation in Oct 2025. *Market Cap:* ~$140M. *Liquidity:* ~200–300k shares/day. *Note:* We considered IOBT due to its sizable upside if the FDA shows flexibility. However, the uncertainty around approval (the trial didn't officially hit its primary endpoint) and the likely longer timeline (a BLA filing, if it happens, would be in 2026) make it less ideal for our immediate needs. It remains on our watchlist, but we **decided not to add** it now.

- **ALDX – Aldeyra Therapeutics** (NASDAQ:ALDX): *Thesis:* PDUFA (Dec 16, 2025) for Reproxalap in dry eye disease, a catalyst we previously were positioned for. *Catalyst:* FDA decision in mid-December. *Market Cap:* ~$318M as of early Oct [15] – slightly above our $300M limit. *Note:* We have exited ALDX earlier to reallocate capital. While the event is significant (and consensus leans positive on approval), Aldeyra's size now breaches our rules for adding new shares. Thus, we will not re-initiate ALDX. We'll monitor the outcome as an external reference for biotech catalyst momentum.

(Other micro-cap biotech names were analyzed but did not make the cut due to either catalyst timing beyond our horizon or insufficient risk/reward. The above list captures the key candidates. MIST clearly stands out and aligns perfectly with our strategy.)

Portfolio Actions

Based on the above assessment and research, here are the planned actions for each holding and new positions:

- **Keep SPRO:** *Action:* **Trim (partial sell) but retain core position.** We will **reduce our SPRO holdings** from 22 shares to 15 shares. This trim is purely for **risk management and rebalancing** – SPRO had grown to ~60% of our portfolio. By trimming ~7 shares, we lower it to ~40% allocation, which is more prudent. We remain bullish on SPRO (NDA filing catalyst and GSK partnership intact), so we want to keep a significant stake. The reason for trimming is to **free up cash** for a higher-immediacy catalyst (MIST) while still participating in SPRO's upside. *Rationale:* SPRO's thesis is unchanged – it's a relatively de-risked antibiotic story with likely FDA approval in 2026 and possibly more GSK milestone news in coming quarters. We simply had to lighten it to adhere to concentration discipline and seize a nearer-term opportunity. We will maintain the **stop-loss at $1.78** on the remaining shares (just under recent lows). If SPRO experiences any unexpected negative developments (regulatory delays, etc.), we'll re-evaluate, but for now it's a firm **hold** (just smaller).

- **Exit OKYO:** *Action:* **Sell all 10 shares of OKYO.** We have decided to **fully exit** this position. *Reason:* OKYO's catalyst is behind us (Phase 2 data were a success, boosting the stock in Q2/Q3 [21]), and while the outcome was positive, the next steps (larger trials, FDA meetings) will take time. With no

major catalysts in Q4 2025 and the stock already retracing, our capital can be better deployed elsewhere. Additionally, OKYO's cash needs for the upcoming 100-patient trial could introduce dilution risk in the interim. Exiting now locks in a small realized loss (~-6%) but **prevents further stagnation**. We will reallocate the ~$19.5 cash from this sale into a more catalyst-rich idea (MIST). OKYO was a strategic play that simply doesn't fit the remaining timeline of our experiment, so we are taking decisive action to optimize the portfolio's catalyst density. (No stop-loss needed anymore as we are selling outright.)

- **Keep TLSA:** *Action:* **Hold position (no change in share count).** We will **continue to hold** our 6 shares of Tiziana Life Sciences. *Reason:* TLSA provides exposure to a *transformative platform* (intranasal immunotherapy) and has strong upward momentum and multiple shots on goal. It balances the portfolio by not being a binary "one-event" stock – its value can grow via incremental progress and it's not tied to a single yes/no decision this quarter. We have confidence in management (demonstrated by insider buying [23] [24]) and in the science (novel approach with encouraging early signals). Although TLSA's big catalysts (e.g. MS trial data) are further out, the **steady news flow** (trial initiations, grants, etc.) should keep investors interested. Also, retaining TLSA ensures we're not 100% concentrated in regulatory events – it's a **diversifier with high long-term upside**. We will keep our stop at $1.78 for downside protection. No trim or add here, as the position size (~15%) is modest and appropriate.

- **Initiate MIST:** *Action:* **Buy a new position in MIST (Milestone Pharmaceuticals).** We plan to **initiate a position** of approximately ~$35 in value, which at current prices is **17 shares** of MIST. *Target Size:* This will be roughly ~42% of the portfolio, making it a top holding alongside SPRO. We are comfortable with that size given the high conviction and near-term catalyst. *Reason:* MIST's upcoming PDUFA on Dec 13 is a catalyst that can potentially **transform our portfolio's performance** if successful. Our research indicates a strong chance of approval since Milestone has addressed the FDA's concerns (which were CMC-related) [10] and even **extended a financing backstop** in anticipation of approval [29]. The PSVT indication has a substantial market (estimated $1B+ by 2030) [30], and MIST's current ~$2 stock price doesn't reflect this – in fact, AInvest's analysis suggests the stock could reach $10–$12+ on approval [31], and even in a conservative scenario analysts see maybe $15–$20 in a squeeze [32]. This is exactly the kind of asymmetric setup we seek. *Catalyst:* FDA decision (approve or reject) by 12/13/25. If approved, the stock could surge (our price target would be in the mid-teens, vs. ~$2 now). If a surprise rejection occurs, downside could be to ~$1 or lower – but given the CRL issues were resolved and the clinical data are strong (no safety concerns, demonstrated efficacy in prior Phase 3), we view that as a smaller probability. In essence, we're risking ~$2/share to possibly make $8-$10/share. This **risk/reward is very compelling** [31]. *Stop-loss:* We will set a stop around $1.70 (about 15% below our entry) to guard against unforeseen sell-offs prior to the FDA decision. (Important: we acknowledge stop losses won't prevent gap-down risk on the binary event, so position sizing is key – we sized it such that even a total loss would be survivable for the portfolio, albeit painful.) Overall, initiating MIST shifts our portfolio toward a high-impact event that occurs before the experiment ends, aligning with our mandate to optimize risk-adjusted return in the short remaining period.

In summary, our actions concentrate the portfolio into **fewer, higher-conviction bets** on upcoming catalysts. We will have **three holdings** post-trades: SPRO (trimmed but kept), TLSA (kept), and MIST (new). OKYO will be fully exited. The rationale is to focus on the names that can drive meaningful portfolio gains in the next ~10 weeks, while cutting those with limited short-term upside. We have also adjusted position sizes

to ensure no rule violations and to manage risk – notably reducing SPRO's weight and spreading capital to MIST. Each action was taken with careful consideration of the catalyst calendar, fundamental outlook, and risk controls.

Exact Orders

The following are the specific orders to execute these portfolio changes. All orders are to be placed at the start of the next trading session (Intended Execution Date: **2025-10-13**). We use limit orders to control entry/exit prices, given the stocks' volatility. (If not filled, we will reassess, but the limits are set near current prices to likely execute.)

1. **Sell Order – OKYO**
2. **Action:** Sell
3. **Ticker:** OKYO
4. **Shares:** 10 (full position)
5. **Order Type:** Limit (DAY)
6. **Limit Price:** $1.95
7. **Time in Force:** DAY
8. **Intended Execution:** 2025-10-13 (next trading day)
9. **Special Instructions:** This limit is set at OKYO's approximate last closing price (around $1.95 [33]). We aim to exit at or above our cost. We will allow partial fills if necessary, but given OKYO's average volume (~117k/day [34]), selling 10 shares should fill easily. No stop-loss is needed anymore once sold.

10. **Rationale:** Exiting OKYO as discussed – to reallocate capital from a now inactive catalyst play to a more immediate opportunity. The limit price ensures we don't sell for less than recent market value, as there's no urgency to dump below fair price. We expect to get filled near $1.95 (or higher if there's an uptick on Monday).

11. **Sell Order – SPRO (Partial Trim)**

12. **Action:** Sell (partial trim)
13. **Ticker:** SPRO
14. **Shares:** 7 (out of 22)
15. **Order Type:** Limit (DAY)
16. **Limit Price:** $2.25
17. **Time in Force:** DAY
18. **Intended Execution:** 2025-10-13
19. **Special Instructions:** This will reduce our SPRO holdings from 22 to 15 shares. The $2.25 limit is just below the recent close (~$2.28 on 10/10) to ensure execution while still getting a fair price. SPRO trades hundreds of thousands of shares daily (e.g. ~380k–800k shares on recent days [35]), so selling 7 shares is negligible volume – we expect an immediate fill at our limit or better. We'll monitor the open; if SPRO is trading higher, we may get a higher price (the limit is a minimum acceptable). The remaining 15 shares will be held with our existing stop.

20. **Rationale:** Trimming to lock in some gains and free ~$15 for redeployment into MIST, as detailed above. We chose 7 shares so that SPRO remains a meaningful ~40% position. The limit order at $2.25

ensures we don't sell into any momentary bid-weakness; SPRO has been trading in the $2.10–2.30 range recently, so $2.25 is a reasonable execution target that reflects its current value.

21. **Buy Order – MIST**

22. **Action:** Buy (Initiate new position)
23. **Ticker:** MIST
24. **Shares:** 17
25. **Order Type:** Limit (DAY)
26. **Limit Price:** $2.10
27. **Time in Force:** DAY (convert to GTC if not filled Day 1)
28. **Intended Execution:** 2025-10-13
29. **Stop Loss:** $1.70 (GTC stop order, ~19% below limit price, to activate after purchase)
30. **Special Instructions:** We are placing a limit slightly above the last closing price ($1.99, with after-hours around $2.04) [33] . This $2.10 cap should ensure we get filled even if there's minor upward fluctuation at the open, without overpaying significantly. We plan to deploy roughly $35.7 of cash (17 * $2.10). If the stock opens much higher (above $2.10) unexpectedly, the order won't fill – in that unlikely case, we would reassess whether to chase or wait. The **stop-loss** at $1.70 will be set once the position is acquired (good-til-cancelled). That stop is about 15-20% below our entry, near recent support levels in the $1.70s. It's meant to limit loss if, for example, broader market sell-off or adverse news hits MIST before the FDA decision. (We acknowledge a stop won't help much *on* the actual PDUFA outcome if negative, due to gap risk, but it's important to have it in place for pre-event trading swings.)
31. **Rationale:** Initiating a substantial position in MIST to capitalize on its Dec 13 PDUFA catalyst. The size (17 shares, ~42% allocation) reflects our strong conviction and the asymmetric payoff potential. We use a limit order to avoid any liquidity spike at market open – MIST is liquid (~1.3M avg volume [27] , 1.7M shares traded last session) so we likely could do a market order, but a limit at $2.10 gives us price control with virtually no risk of missing the trade. This buy will significantly increase our portfolio's exposure to an event-driven upside. The stop-loss is a prudent safety measure against unforeseen downside prior to the decision. Overall, this order executes our plan to "swap" the capital from OKYO (and a slice of SPRO) into MIST, thereby increasing our portfolio's catalyst immediacy.

(All orders are DAY orders (except the stop), intended for execution on 2025-10-13's regular session. We assume standard trade execution policy – i.e., limit orders will fill up to the limit price or better, or not at all by day's end. We selected limit orders due to the volatile nature of micro-caps, to avoid slippage. If any order does not execute (e.g., if MIST doesn't dip to $2.10 and we chose not to chase higher intraday), we will revisit the strategy promptly.)

Risk and Liquidity Checks

Post-Trade Portfolio Composition: After these trades, our portfolio will consist of 3 stocks: **SPRO (~15 shares), TLSA (6 shares), MIST (17 shares)**, plus a minimal cash reserve (~$0.3). The approximate weights will be MIST ~42%, SPRO ~42%, TLSA ~15%, cash <1%. This is a **concentrated portfolio**, which is an intentional risk stance given the high-conviction catalysts ahead. We acknowledge the concentration risk – two positions make up ~84% – but we have mitigated it by selecting uncorrelated catalysts (antibiotic approval, cardiac drug approval, neuro-immunology platform) and by using stop-loss orders. No single position violates any explicit constraint (we have no rule against a 40% position, and we have deemed it

acceptable given our short horizon and need for upside). We will monitor this closely; if any one holding starts exceeding a comfortable threshold due to price movement, we might rebalance as needed.

Cash After Trades: We will essentially be fully invested. Before trades, cash was $0.56. Selling OKYO and 7 SPRO shares will **raise about $35.5** (OKYO $19.5 + SPRO ~$15.9)【40†】. Using ~$35.7 to buy MIST will leave roughly **$0.3 in cash** (essentially just a rounding remainder). This near-zero cash is acceptable as we're deploying idle cash to go after catalyst-driven alpha. We will keep track of this small cash for any fees or future minor adjustments. **No new capital** was added – we strictly used internal funds, consistent with budget discipline.

Market Cap Compliance: All holdings remain within our micro-cap limit: SPRO ~$126M [18], TLSA ~$234M [25], MIST ~$200M [9] as of recent data. We are not adding any name that breaches the $300M cap rule. We explicitly avoided ALDX due to its ~$318M cap [15]. We will re-check market caps each week to ensure ongoing compliance (if, say, TLSA appreciates and crosses $300M, we know we cannot add more; currently it's safely under).

Liquidity and Order Sizing: The planned trades are very small relative to each stock's trading volume, so we expect **minimal market impact** and easy execution:
- *OKYO:* 117k average daily volume [34]; we're selling 10 shares (<<1% of daily volume).
- *SPRO:* ~400k+ average volume (e.g. 748k shares on 10/7) [35]; selling 7 shares is trivial (<0.002% of daily volume).
- *TLSA:* ~300–600k daily volume (612k on 10/10) [36]; we are not trading TLSA this week (just holding). Our existing 6 shares are ~0.001% of daily vol – highly liquid.
- *MIST:* ~1.3M average volume (1.7M on 10/10) [27]; buying 17 shares is <0.002% of daily volume.

These figures confirm **excellent liquidity** for our order sizes. We do not anticipate any slippage beyond a few pennies. We set limit prices near current quotes to further ensure we don't get poor fills. There is no concern about being able to enter or exit these positions promptly if needed.

Stop-Loss Placements: After trades, we will have stops on all three positions: SPRO @ $1.78, TLSA @ $1.78, MIST @ $1.70. Each stop is chosen to be ~10–20% below the current price, typically just under key support levels or our cost basis. This limits our downside in normal trading conditions. It's important to note that for binary event stocks (MIST, and eventually SPRO next year), gap risk exists – a bad FDA outcome could drop the price far below the stop before it triggers. We accept that risk; the stops are primarily to guard against non-catalyst-related declines or a loss of momentum that might indicate changing conditions. We are **prepared to override stops** or adjust them if new information suggests doing so (for instance, if MIST runs up significantly before approval, we might raise its stop to protect profits).

Risk of Breach and Mitigation: No risk limits are currently breached. Position sizes are elevated by design, but all within experimental allowances. We have no leverage, no shorts, and our cash usage is within available funds. The main risk to highlight is that we now rely on a couple of big events – this could lead to volatility. To manage this: (a) We will monitor news like hawks – any early signs of trouble (e.g. FDA extension requests, unexpected delays) and we would reconsider our positions quickly; (b) We might realize partial gains ahead of an event if the stock runs up excessively (reducing exposure so that we "play with house money" to an extent). In the case of MIST, for example, if it jumps to $4-$5 before Dec 13 on speculation, we could take some profit off to lower binary risk. We will also keep an eye on macro factors –

broad market sell-offs can hit small caps hard, and we'd be ready to tighten stops or temporarily hedge (though our rules forbid direct hedging with derivatives, the stops are our main hedge).

In summary, after these adjustments the portfolio is **tightly aligned to catalyst outcomes**. Liquidity is ample for all positions/trades. We've concentrated risk in a calculated way, and we've put safety nets (stops) to catch normal downside moves. The risk profile is elevated (as expected in a micro-cap catalyst strategy), but we judge it appropriate given the potential rewards and the shrinking timeframe to meet our objectives. We will continuously reevaluate risk each week and will not hesitate to make further changes if any position's risk/reward deteriorates.

Monitoring Plan

Over the coming week (and beyond), we will implement a strict monitoring regimen for our portfolio:

- **Daily News & Filings Check:** Each morning and evening, we will scan for news on SPRO, TLSA, and MIST. This includes press releases, SEC filings, and credible media coverage. For MIST in particular, we'll watch for any FDA communications (e.g. mid-cycle review updates, label discussions) – although none are explicitly expected pre-PDUFA, sometimes analysts publish notes or the company issues updates. For SPRO, we'll look out for an announcement of the **NDA submission** to the FDA (which should happen in Q4 per guidance [1]). While NDA filing itself may not skyrocket the stock, it's a de-risking milestone that could improve sentiment. For TLSA, we expect a relatively steady flow of incremental updates – e.g. enrollment progress in trials, possibly a scientific conference abstract. We know on Sept 24-26 TLSA presented a poster at ECTRIMS (an MS conference) about their trial design [37]; any feedback or investor reactions from that will be noted. We'll also track if any **analyst research** or biotech newsletters comment on our names, as that can move micro-caps.

- **Price and Volume Alerts:** We will set automated alerts for significant price moves (e.g. >5-10% intraday swings) or unusual volume in our stocks. Given the volatility of micro-caps, sudden moves can happen – if MIST, for example, spikes 20% on a rumor, we want to know immediately and assess whether to adjust our position (perhaps trim a bit into strength). Conversely, if any position falls toward its stop-loss, we'll pay close attention – a drop on high volume might indicate news we need to investigate (before the stop potentially triggers). Specifically, if SPRO or TLSA approach their $1.78 stops, we'll try to ascertain if it's market noise or a fundamental issue (e.g. bad news from a competitor's trial in a similar field, etc.) and decide if we let the stop execute or intervene. The stops are GTC, so they'll execute if reached; we'll be monitoring in real-time to ensure we make an informed decision rather than a blind stop hit in case of a temporary dip.

- **Macro and Sector Watch:** We will monitor the overall biotech sector sentiment (XBI index, etc.) and any macro news that could affect risk appetite. Our portfolio is entirely biotech micro-caps now, which means it's sensitive to sector rotations and financing environment news. For instance, any hints of FDA being more strict or any high-profile FDA decisions in Q4 (like the Iovance or Aldeyra outcomes) could impact sentiment for our approvals. We'll watch the outcome of other PDUFAs around the same time (e.g., IOVA's and ALDX's in mid/late Dec) as read-through. If we see a broad small-cap biotech sell-off or rally, we may adjust our exposure accordingly (though likely our positions would move with the tide).

- **Catalyst Game Plan:** For each catalyst, we will formulate a detailed plan ahead of time:

- *MIST:* We will decide by early December whether to hold through the PDUFA or take profit beforehand. Current leaning: if the stock is still in the ~$2-3 range, we likely hold through the decision because the upside on approval is so high. If the stock runs to, say, $5+ pre-event (on speculation or hype), we might sell a portion to secure gains and reduce binary risk. We will also watch for any signs of an FDA advisory committee or label concerns. (FDA did *not* plan an AdCom as of acceptance [38], which is good.) We expect to see an FDA approval decision by Dec 13 (a Sunday, so effectively by Friday Dec 12 or Monday Dec 15). We'll be on high alert that week – ready to react the morning after the news: if approved, likely let winners run initially; if a CRL, immediately preserve remaining capital (though at that point stops would likely trigger).
- *SPRO:* The SPRO catalyst (NDA filing) is less binary. If/when they announce the NDA submission (could be any time in Q4), we'll gauge market reaction. A spike on that news could be an opportunity to trim a bit more if the position swells, but we also see SPRO as a longer-term hold (beyond the experiment) with possibly bigger gains as approval nears in 2026. Since our experiment ends Dec 27, we may consider exiting SPRO in late December if it hasn't moved, to avoid holding into 2026 catalyst beyond our horizon – however, we'll decide that as we approach the end, depending on performance and any better uses of capital. For this week, we simply monitor SPRO's trading and any GSK-related news (e.g., GSK might mention tebipenem in a pipeline update or a conference).

- *TLSA:* While no binary event is slated for Q4, we'll watch for **scientific updates** (perhaps initial read on safety/tolerability from the ongoing trials if they release any interim updates, or additional case reports like the Alzheimer's patient data). Tiziana's management tends to issue updates regularly. We will also watch the stock technically – it's been consolidating around $2. If it breaks out above the $2.50 high on volume, that could signal another momentum run (perhaps on speculation of partnership or just year-end small-cap rotation). In that case, we might ride the momentum and raise the stop to protect profits. Conversely, if it drifts down without news and hits our stop, we'll re-evaluate the thesis vs. the need to protect capital.

- **Weekly Portfolio Review:** During each weekend's deep research window, we will reassess each holding's thesis in light of the week's events. We'll check if any **stop-loss adjustments** are warranted (for example, if MIST moves up to $3-$4, we'd likely tighten its stop to lock in at least break-even or better). We will also look for any new opportunities that might emerge (the biotech space can always surprise – e.g., if a micro-cap crashes on overreaction and still has a catalyst, or if new PDUFA dates are announced). However, given the short time left, our bias is to stick with what we have unless something clearly superior appears.

- **Risk Management Actions:** If any position violates our risk parameters or something changes (e.g., a delay in MIST's FDA decision gets announced – hypothetically pushing it to 2026, which would kill our thesis for the experiment's timeframe), we will act immediately, not wait for the next window. Specifically:

- If MIST's story changes (though unlikely at this point), we'd exit to avoid holding through a now unfavorable risk.
- If TLSA or SPRO were to skyrocket and exceed the $300M cap threshold significantly, we wouldn't add more, but we might consider trimming if valuation overshoots fundamentals.
- If any stop is triggered, we will log the reason and decide whether to re-enter or stay in cash.
- We'll also ensure no **new violations** of rules occur – e.g., if an announced share count change pushes market cap over $300M for a holding, we'll note it.

Contingency Plans: We recognize that micro-cap biotech is volatile. We have structured stops and position sizes to prevent a single event from ending the game, but multiple adverse outcomes could still hurt. In a worst-case scenario (e.g., MIST CRL and a broad biotech drop), our portfolio could draw down significantly. Our contingency in that case (with just weeks left) would be to possibly pivot any remaining assets to a very safe or benchmark-like holding to preserve capital (though given the experiment's nature, we likely will stick with catalysts). Conversely, in a best-case scenario (MIST approval and big jump), we will likely take some profits and perhaps redeploy into another late Q4 catalyst or even hold some cash to secure our lead against the benchmark.

In sum, **active monitoring and agility** will be key. We will stay on top of all relevant information and be ready to make intra-week decisions if needed. The plan is to let our catalysts play out, but always with an eye on managing downside. This coming week specifically, the focus will be on **executing our trades smoothly** (ensuring MIST position is established) and then tracking any early signals on MIST's FDA review progress or SPRO's NDA steps. We will report back on any material changes or decisions made during the week.

Thesis Review Summary

By rebalancing the portfolio in Week 16, we have sharpened our focus on high-impact, near-term catalysts while shoring up risk controls. We enter the coming weeks with **three distinct biotech bets**:

- **Milestone Pharmaceuticals (MIST)** – our new, highest-conviction position – epitomizes the portfolio's swing for asymmetric rewards. MIST's December 13 FDA decision for its PSVT nasal spray is a catalyst with the potential to **dramatically boost our portfolio's value** if approved. We've done the homework: the CRL issues were addressed [10], and the therapy could fill a genuine unmet need in cardiology (treating rapid heart arrhythmias at home). At a ~$200M valuation, the market is skeptical, but we believe this is a classic case of a beaten-down micro-cap poised for a comeback. Our thesis: If the FDA greenlights etripamil, Milestone's stock could multiply (analysts suggest a move to the teens per share on approval [31]). That would not only close our performance gap with the S&P, it could put us well ahead. We've allocated boldly here (~42% of portfolio) to maximize the benefit if our thesis proves correct – all while being mindful of the downside (a stop is in place, and position size is such that a total loss, while damaging, would not zero out the portfolio).

- **Spero Therapeutics (SPRO)** – our steady performer and previous top holding – continues to anchor the portfolio with a somewhat lower-risk catalyst on the horizon. SPRO's partnership with GSK and the upcoming NDA submission for its oral antibiotic give it a **fundamentally strong foundation** [1]. We trimmed the position to fund MIST, but we remain confident in SPRO's value. This is the "slow-burn" catalyst in our basket: the stock may appreciate gradually as regulatory milestones are met (NDA filing acceptance, etc.) and as investors recognize the 2026 approval opportunity. Importantly, SPRO provides a bit of diversification: unlike MIST (which is binary in the next 2 months), SPRO's catalyst is on a longer timeline and its downside is cushioned by the fact it has a major pharma partner and cash runway. Our thesis for SPRO is unchanged – by the experiment's end, we may not see explosive moves, but we expect a positive bias in the stock price as the NDA news comes out. And beyond this experiment, SPRO has all the hallmarks of a multi-bagger (a tiny cap addressing a large need with Big Pharma backing). For now, it remains a core hold, just right-sized.

- **Tiziana Life Sciences (TLSA)** – our innovative wild card – adds thematic diversity and a momentum play to the portfolio. TLSA's intranasal foralumab is **pioneering a new route of immunotherapy** for neurodegenerative and autoimmune diseases. Our thesis has been that Tiziana's numerous "irons in the fire" (MS, ALS, Alzheimer's, etc.) and its novel delivery method could attract increasing investor and possibly partner interest. The stock's year-to-date performance (+200%+) and continued positive updates validate that thesis [5] [39]. While TLSA won't have a binary event during our experiment, we expect its strong news flow to continue – acting as a catalyst in its own right by keeping the stock on an upward trajectory. In the next weeks, any additional data or even speculation of a partnership (not uncommon for a company with such a platform) could lift the stock. We've kept the position smaller, reflecting its medium-term horizon, but we view TLSA as a **high-upside, moderate-risk** component. It balances the portfolio by not being purely dependent on FDA decisions; it has a pipeline story that could independently create value. Our stop-loss will protect us in case the momentum abruptly reverses, but otherwise we plan to ride the trend. The thesis: Tiziana's approach could be paradigm-shifting (e.g., an MS therapy that is nasal rather than IV) – that promise should continue to attract investor attention into year-end, especially as micro-caps start to recover sector-wide.

In summary, our portfolio realignment leaves us with a concentrated yet we believe **well-considered trio** of positions. We have one near-term binary catalyst (MIST – FDA decision), one mid-term catalyst with long-term multi-bagger potential (SPRO – NDA/approval with GSK support), and one innovative growth story (TLSA – multiple trials and steady news). All three are trading at valuations that, in our analysis, **do not fully price in their upside potential**. We have effectively increased the portfolio's "beta" to biotech catalysts – a necessary move given we are currently behind the benchmark ($81.8 vs $105.6 from $100 start) and have limited time to catch up [40]. This comes with higher risk, but our risk management tools are in place: position sizing (we spread bets across three names), stop-loss orders, and diligent monitoring.

The upcoming week will be focused on executing our plan and then patiently tracking our theses as they play out. If our convictions are right, we could see a significant upswing in portfolio value in the coming weeks – MIST's run-up or approval, continued drift up in TLSA, and a stable-to-rising SPRO. We are aware that the opposite could happen (negative surprises), but we've accepted those risks as part of the experiment's mandate to seek alpha in micro-caps. Each position has a clear rationale tied to real upcoming events or data: **no "story stock" without substance** is in our book now.

We'll remain nimble – ready to adjust if needed – but as of now, the strategy is set: **concentrate on the best catalysts, protect the downside, and let the upside work for us**. With this approach, we aim to close the performance gap and finish the experiment strong. The groundwork has been laid; now we let the biotech catalysts (and perhaps a bit of luck) determine the outcome.

(Benchmarks & Metrics: Current portfolio value $81.80 vs ~$105.60 if in S&P 500 [40]. Our reshuffle is high risk/high reward in an attempt to bridge that ~22% gap. We believe the selected catalysts give us a fighting chance. We will update on progress next week, with a close eye on any thesis changes.)

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