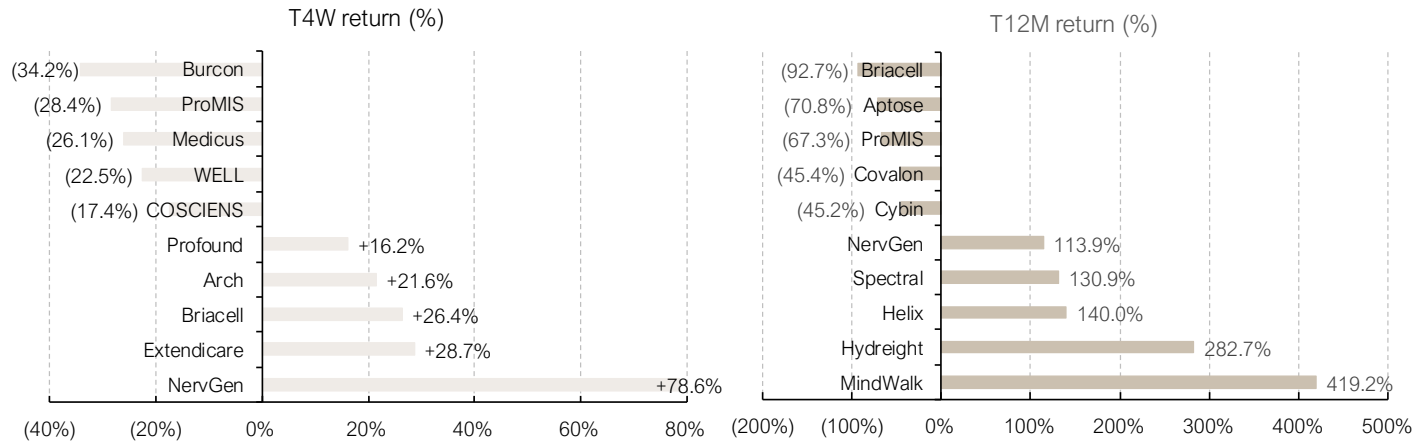
Core Highlights of the Week

Top Movers

Exhibit 1. Top Healthcare/Biotechnology Movers for the Trailing Four-Week & YTD Periods



Source: Leede Financial, Refinitiv

Updates From Our Coverage Universe

- **Cardiol provides Phase II update for its ARCHER acute myocarditis trial.** ON-based cardiovascular disease-focused small-molecule drug developer Cardiol Therapeutics (CRDL-T, Spec Buy, C$7.00) provided an update on clinical performance of the firm's ultrapure orally-active anti-inflammatory cannabidiol formulation CardiolRx in the 109-patient Phase II ARCHER acute myocarditis trial. Our revised PT is now based on NPV (25% discount rate) & multiples of our F2031 adjusted EBITDA/fd EPS projections, as we described in a Cardiol-specific report earlier this week.
    - We revised our valuation for CRDL in response to that update, not because we believe that ARCHER data was negative despite not quite hitting statistical significance for the trial's two co-primary endpoints based on impact on structural heart measures (cardiac MRI-confirmed changes in extracellular volume [a well-established measure of inflammation & fibrosis in cardiac tissue] or in global longitudinal strain [a MR-assessable measure of left ventricle function]) but rather because it was clear to us from Cardiol's commentary that ARCHER now has secondary if not tertiary priority in the firm's suite of clinical activities going forward. No discussion of timelines to engaging with the US FDA on contemplating Phase III acute myocarditis study design, or any interest in doing so, was forthcoming.
    - Other secondary endpoints showed more favorable impact from CardiolRx administration over the twelve-week study, including on two other measures of heart pathology (left ventricle mass, which seems to us to be an equally credible measure of left ventricle pathology as any of the co-primary endpoints, & left atrial end-systolic volume) & we indicated in our most recent CRDL report that we believed that ARCHER data when considered in aggregate were sufficiently positive to justify future Phase III testing for the indication.

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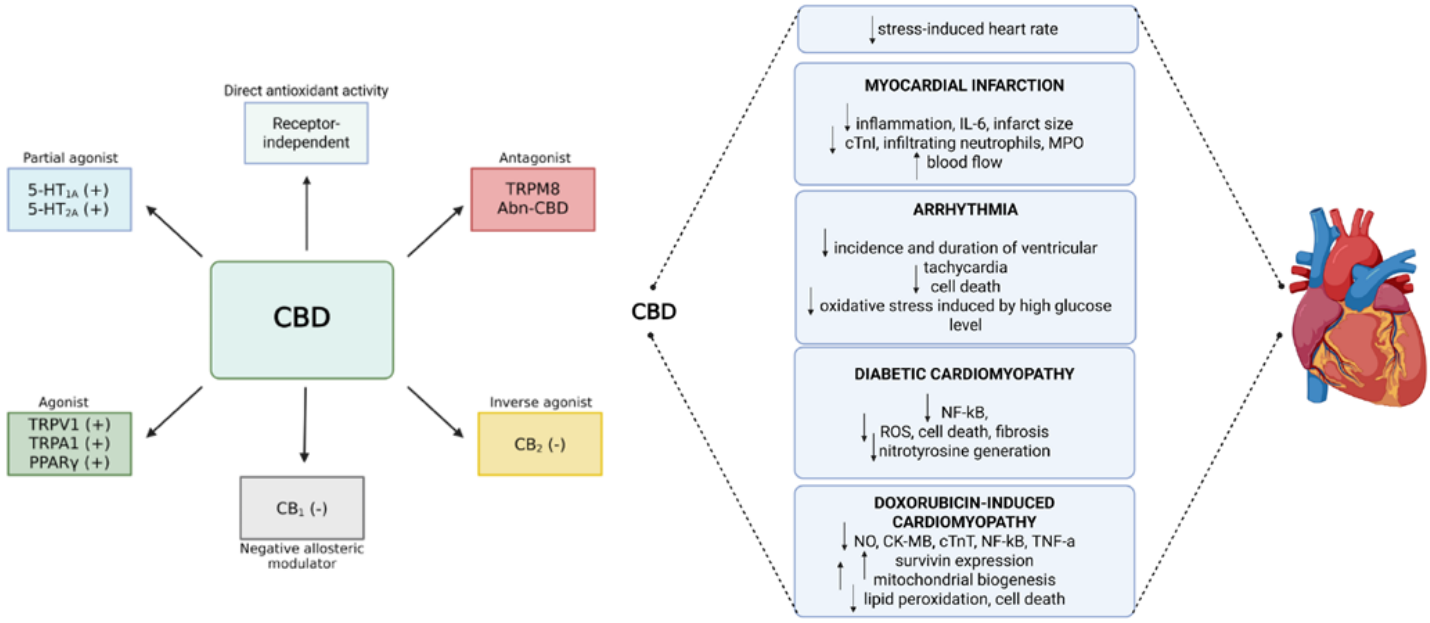
- But we inferred from Cardiol's conference call commentary that it sees ARCHER data as more mechanistically-validating for CardiolRx's prospects in other cardiovascular indications, mainly recurrent pericarditis for which the 110-patient Phase III MAvERIC trial is ongoing & in diastolic heart failure for which IND-enabling testing of an injectable cannabidiol formulation CRD-38 is ongoing & poised to support formal IND submission & commencement of Phase I/II heart failure testing next year.
- In our note, we described our revised CardiolRx royalty revenue projections that now assume that the drug could be FDA-approved for acute myocarditis by FH231 (previously FH229), during which we project myocarditis-specific royalty revenue from future partner(s) of C$33.6M, increasing to C$84.4M in F2032 & to C$101.9M in F2033. But we consider our myocarditis-based royalty revenue forecasts to be at greatest risk in our model, pending Cardiol's own cautious commentary on its path forward (or lack thereof) in this indication.
- Our model still assumes that Cardiol will focus on recurrent pericarditis as a flagship CardiolRx indication, for which our royalty revenue forecasts were unchanged (C$32.6M in F2029, C$82.0M in F2030, C$107.2M in F2031), with diastolic heart failure (HFpEF, a left heart pathology whereby the left atrium inefficiently pumps oxygenated blood into the left ventricle, as distinct from congestive heart failure in which the left ventricle inefficiently pumps oxygenated blood into systemic circulation) still a focus for the firm's elastomer-based subcutaneously-injectable cannabidiol formulation CRD-38; IND-enabling preclinical & foundational pharmacology testing is ongoing & our model assumes that both IND filing & commencement of formal Phase I HFpEF testing can commence in F2026.
- Diastolic heart failure is the largest cardiovascular medical market to which we ascribe value in our model, in which we project peak CRD-38 royalty revenue from future partner(s) of C$154.0M by F2035. Novartis' (NVS-NY, NR) valsartan/sacubitril combination drug Entresto generated FQ325 sales of US$1.9B, though we assume that generic competition (specifically though not exclusively from NJ-based MSN Laboratories [private]) could dampen quarterly sales going forward, incentivizing Novartis to actively seek out alternative Rx therapies to stabilize its Cardiovascular, Renal & Metabolic division.

Exhibit 2. Even Before Considering Cardiol's Own Data On Cannabidiol's Inflammasome-Mediated Anti-Inflammatory Activity, Other Researchers Document Other Cardiovascular-Relevant Pharmacology for The Drug



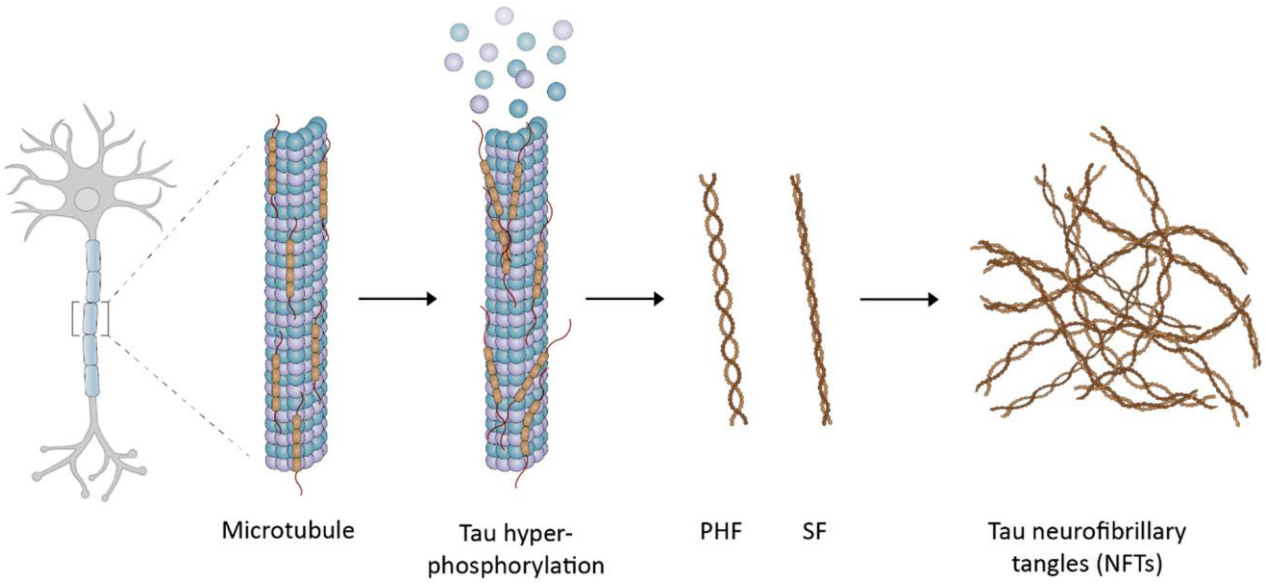
Source: *International Journal of Molecular Sciences (2025). Vol. 26, pp. 9610-9628.*

- On the milestone watch, we are focused on timelines to completing patient enrollment in the 110-patient placebo-controlled six-month Phase III MAvERIC trial, in which CardiolRx monotherapy will be assessed on patients who for one reason or another have discontinued treatment with Kiniksa's (KNSA-Q, NR) leading interleukin-1-blocking biologic rilonacept/

Arcalyst, for which FQ325 sales were US$180.9M & still growing aggressively (up 61% y/y) in a niche cardiovascular medical markets that is clearly no longer quite so niche with standard-of-care already generating run-rate revenue exceeding US$720M. MAvERIC patient enrollment commenced in Apr/25 & primary six-month efficacy data (disease recurrence rate, change in NRS pain score from baseline) are expected by FQ426. While on the topic of Kiniksa & recurrent pericarditis, the firm is separately funding a Phase II academic-sponsored (Mayo Clinic, Johns Hopkins University) rilonacept trial in cardiac sarcoidosis (interestingly, no rilonacept acute myocarditis testing is ongoing) while a next-generation interleukin-1 antagonist mAb KPL-387 is undergoing recurrent pericarditis testing in a 165-patient placebo-controlled trial for which primary six-month efficacy data are expected by end-of-F2027.

- **ProMIS Neurosciences & its R&D team publishes insight into how phosphorylated tau protein serves as a diagnostic marker for Alzheimer's disease, including as a marker for performance of its own amyloid oligomer-targeted PMN310.** MA-based CNS disease-targeted biologics developer ProMIS Neurosciences (PMN-Q, Spec Buy, PT US$9.50) & its scientific team co-authored an Alzheimer's disease diagnostic biomarker study this month in the journal *Alzheimer's & Dementia*, nicely showing therein that two variants of the neurofibrillary tangles protein tau were tightly correlated with disease, as independently diagnosed with a more functional cognitive measure, the Clinical Dementia Rating scale.
  - The two forms of tau that were identified to be tightly correlated with Alzheimer's disease symptoms were phosphorylated tau versions called pTau 181 & pTau 217, one of which is phosphorylated at the hydroxyl group on the amino acid threonine at position #181 of the tau amino acid chain & the other is phosphorylated at a different threonine residue, predictably found at position #217 within the tau amino acid chain. Tau itself is a protein found in microtubules that reside in all cell types including neurons & which can be triggered to become hyperphosphorylated & in so doing, can self-aggregate into so-called tau neurofibrillary tangles that may themselves not just be diagnostic of Alzheimer's disease but also directly contribute to its pathology in ways that are still being explored. Many clinical studies are ongoing that are testing tau-targeted biologics, as we described in prior Healthcare Weeklies & in our ProMIS initiation report.

Exhibit 3. Though ProMIS Is Clearly Testing A Unique Theory On Alzheimer's Disease Pathology Based On Targeting Amyloid Oligomers, Tau Biology Is Now Well-Established As Being Relevant To Disease Diagnosis



Source: *Pharmaceuticals (2021). Vol. 14, pp. 110-122.*

- To be clear, the utility of pTau181 & pTau217 is not exactly new science, with both biomarkers well-known to be associated with onset of cognitive impairment, but the technical challenge was to conclusively show that serum levels of either or both proteins were correlated with cerebrospinal fluid-residing levels of these biomarkers, & of course to show that either or both could be shown to differentiate between different forms of cognition in a reproducible way. Both pTau 181 & pTau 217 are in fact already the main serum biomarker that forms the basis for Roche's (ROG-SW, NR) blood-based electrochemiluminescence immunoassays Elecsys Phospho-Tau (181P) Plasma & Elecsys pT217p RUO

assays, which Roche runs on its automated cobas platform. Roche received the CE Mark for European approval of Elecsys pTau181 in Jul/25. The pTau217 test was granted Breakthrough Device Designation by the US FDA in 2024.

- The utility of plasma pTau181 specifically was published in *The Lancet* last year in a comprehensive 991-patient study conducted by Spain-based researchers, showing in that study that plasma-based pTau181 exhibited an ROC curve correlation with beta-amyloid of 0.77, quite high by the standard of diagnosing central nervous system disorders (this would be low for an infectious disease, but would be solid performance for a cancer diagnostic, for example), & the corresponding ROC curve for mild cognitive impairment associated with Alzheimer's disease vs non-Alzheimer's disease was even higher at 0.89. pTau181-based test sensitivity was 93.57% while test specificity was lower at 72.38%. Results were also tightly correlated between pTau181 found in cerebrospinal fluid (analysis of which is not amenable to rudimentary screening) & in blood plasma (which is). pTau181 could also be visualized in the brain itself by PET imaging but that technology is not really amenable to routine screening either because it is cumbersome, costly, requires proximity to sources of positron-emitting isotopes (specifically to tau-targeted radiopharmaceuticals like fluorine-18-labeled flortaucipir [FDA-approved as Tauvid by Eli Lilly (LLY-NY, NR) in May/20]) or some combination of all three.

- And going back a few years, a global research consortium that included scientists at Eli Lilly published a pTau217-specific paper in 2020 in the *Journal of the American Medical Association (JAMA)* showing in a 1,402-patient study that plasma-derived pTau217 was even more tightly correlated with Alzheimer's disease than pTau181 or other tau-based markers like neurofilament light chain (NfL), with an area-under-curve (AUC, a measure of test accuracy) of 0.96 in its ability to discriminate Alzheimer's disease from other forms of neurocognitive impairment.

- It was not superior to testing for pTau217 in cerebrospinal fluid or to PET imaging using tau-targeted contrast agents like flortaucipir but the point of the study would not have been to show superiority to these assays but rather to show comparability using blood plasma as the assessable tissue, a far more logistically feasible modality for broad population screening for disease. A separate 2021 study published in *JAMA Neurology* in which Eli Lilly researchers also participated reached a similar conclusion on the utility of plasma-based pTau217 analysis. The studies cited above are not the only studies espousing the virtues of pTau181/pTau217 in Alzheimer's disease, & we cited them for their representative utility & for their corporate sponsorship by pharmaceutical firms with well-established CNS franchises.

- But shifting back to ProMIS' recent contribution to the pTau181/pTau217 diagnostics literature, in the Alzheimer's & Dementia paper, ProMIS & its collaborators showed in a meta-analysis of the existing medical literature that plasma-based levels of both pTau181 & pTau217 & functional measures of cognitive impairment (the Clinival Dementa Rating scale – Sum of Boxes [CDR-SB] test, as indicated above). The meta-analysis used published clinical data from Eisai's (4523-JP, NR) CLARITY-AD trials on which lecanemab/Leqembi's FDA approval was based, as well as data from Biogen's (BIIB-Q, NR) EMERGE/ENGAGE trials on which aducanumab/Aduhelm's FDA approval was based (the mAb has since been voluntarily withdrawn from the US market by Biogen), from Eli Lilly's (LLY-NY, NR) TRAILBLAZER-2 & TRAILBLAZER-ALX trials on which donanemab/Kisunla FDA approval was based & on Roche's (ROG-SW, NR) GRATUATE I & GRADUATE II trials that tested gantenerumab/RG1450 (the mAb failed its primary endpoint, but Roche is now developing a Brainshuttle-modified gantenerumab form called trontinemab that crosses the blood-brain barrier with a transferrin receptor-binding Ab-based modality).

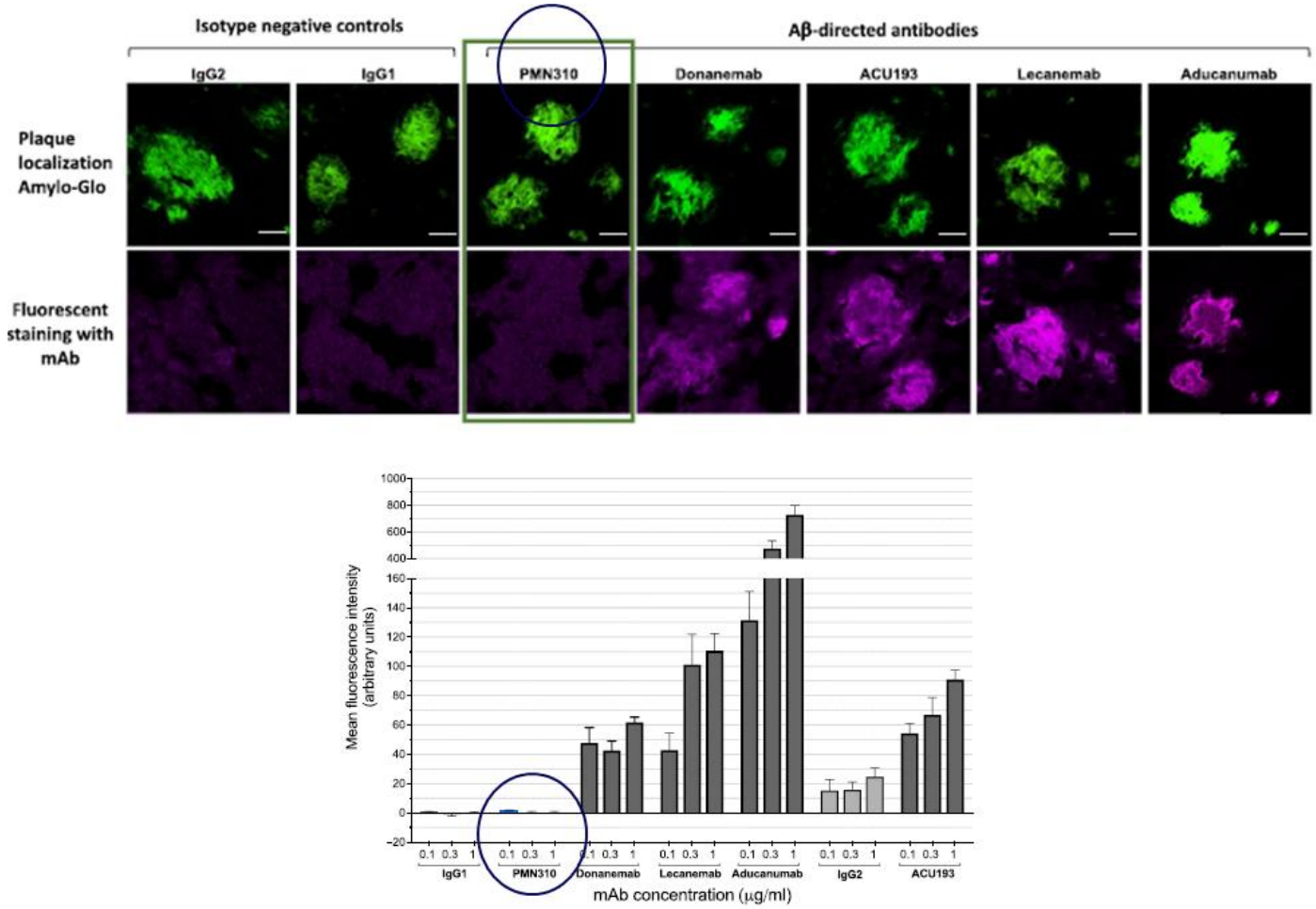
- We endorse the conclusions published in the ProMIS study, though the implications of the conclusions reached in the publication are certainly not unique to ProMIS or its ongoing testing of amyloid oligomer-targeted PMN310 in the PRECISE-AD trial. But there are a few ways that the published meta-analysis is directly if not uniquely relevant to ProMIS/PMN310, including:

    - The study specifically focused on the relationship between plasma pTau181/pTau217 as assessed at six month follow-up & functional cognitive measures that were assessed at a later one-year timepoint. This is directly relevant to PRECISE-AD study design, for which the 128-patient Phase II trial is assessing multiple biomarker & functional cognitive endpoints at one-year follow-up, but with an interim analysis of biomarkers at six months (probably some time in FQ226). It seems unlikely to us that impact on cognition would be observable in a study this modestly-sized at six-months (we ourselves have never seen data from a Phase II/III Alzheimer's disease study showing cognitive improvement over this timeframe), so we believe ProMIS is seeking to provide context for the relevance of its forthcoming interim biomarker-based analysis of PRECISE-AD in a few quarters. Indeed, the firm's intentions on this theme are clear in its press release this week announcing the *Alzheimer's & Dementia* publication.

- It is clear from ProMIS' meta-analysis that changes in pTau181/pTau217 at an interim six-month timepoint did indeed correlate well with shifts in cognitive impairment observed at a later one-year timepoint, with an effect size of 2.6x, thus justifying & enhancing the significance of the planned interim biomarker analysis of PRECISE-AD described above. We of course do not believe that analyzing tau biology is in any way a substitute for direct clinical impact on cognition for any experimental Alzheimer's disease therapy, but ProMIS' meta-analysis of historic clinical data for predecessor amyloid-targeted mAbs does augment the justification for conducting interim biomarker analysis as a way to signal the potential for observing clinical impact on disease symptoms down the road.

- As an aside, we would be remiss not to observe that broader capital markets are clearly casting a skeptical eye toward publicly-traded firms focused on developing amyloid oligomer-targeted biologics, with ProMIS itself trading essentially at its cash value as of this writing & its MA-based peer Acumen Pharmaceuticals (ACOS-Q, NR) is trading at close to cash value with an EV of only US$20M. Acumen's own amyloid oligomer-targeted mAb ACU193/sabirnetug is a bit more advanced than PMN310 & interim Phase I/II data from the 62-patient INTERCEPT-AD are already in the public domain. Acumen is currently funding the 542-patient Phase II ALTITUDE-AD trial for which interim 80-week impact on cognition (assessed by several validated measures of cognitive impairment like the Integrated Alzheimer's Disease Rating Scale, among others) should be reported by end-of-F2026.

Exhibit 4. Unlike Other Clinical-Stage Or FDA-Approved Amyloid-Targeted mAbs, PMN310 Exhibits No Binding To Amyloid Plaques In The Brain, Mitigating Potential For Any Localized Brain Swelling That Such Binding Could Cause



Source: *Pharmaceuticals (2021). Vol. 14, pp. 110-122.*

- Our ongoing diligence on the utility of targeting amyloid oligomers with cognition-reversing therapies, which we stand by, shows us that the concept still holds medical promise in our view, notwithstanding capital market disagreement with us on this theme. As we described in our original PMN report, compelling population genetics studies showed previously that patients harboring specific point mutations for which only amyloid oligomers & no other amyloid form could be created still suffered from cognitive impairment when such oligomers were found in their cerebrospinal fluid; animal studies also showed that amyloid oligomers exhibit their own unique neurotoxicity, distinct from any neurotoxicity that amyloid monomers or fibrils or plaques may confer.

- In a study separately published by ProMIS & its collaborators at the University of British Columbia just last month (coincidentally also in the journal Alzheimer's & Dementia), comparative data showed that of all clinical-stage amyloid-targeted mAbs, PMN310 was shown to exhibit the least binding to amyloid monomers, while still showing potent reversal of cognitive impairment in preclinical models of disease & without any binding to brain-residing plaques that can give rise to localized brain swelling/edema (see Exhibit 4 above). We stand by our Spec Buy on PMN, while mindful that interim biomarker data in FQ226 may be necessary to convince the broader market of the rationale for targeting amyloid oligomers in preference to other disease-relevant targets.

- **Profound Medical signals re-invigorated focus on BPH with TULSA-AI launch.** ON-based medical technology developer Profound Medical (PRN-T/PROF-Q, Buy, PT US$15.25) is actively marketing its FDA-approved MR-guided ultrasound ablation localized prostate disease-targeted platform TULSA-PRO in the US & global markets; in parallel, the firm just announced that it intends to feature the device more aggressively as a therapy for benign prostatic hyperplasia, a distinct endocrinologic prostate disorder that is less severe than localized prostate cancer on which TULSA-PRO's original PMA filing was based (the 110-patient TACT trial assessed TULSA-PRO impact on serum PSA levels in patients with localized prostate cancer, not BPH).

  - Specifically, the firm is launching a new AI-enabled module for optimizing ablation protocols to reduce the size of the prostate gland in BPH patients, as opposed to ablating specific tumors residing within the prostate gland in patients with cancerous or precancerous prostate pathology. The module was featured this week at the annual RSNA meeting in Chicago that we have attended in prior years. Along with this AI/BPH announcement, Profound provided details on other TULSA-PRO-specific marketing initiatives it expects to undertake at RSNA, including featuring that data from its ongoing 201-patient CAPTAIN trial that is expected to generate data next year.

  - The trial is designed to assess impact on disease recurrence & safety profile for TULSA-PRO ultrasound ablation in comparison to radical prostatectomy (presumably in most cases undertaken using Intuitive Surgical's [ISRG-Q, NR] da Vinci surgical robot). There is virtually no probability that TULSA-PRO could out-perform radical gland removal on localized disease recurrence, but we already know that the device performed well at interim analysis on various measures of quality of life & morbidity, including duration of hospital stay post-procedure among other endpoints.

  - Profound shared specific data on relative proportion of TULSA-PRO procedures conducted in FQ325 for BPH vs localized prostate cancer & the proportions do favor prostate cancer by a considerable margin (79% of procedures for prostate cancer vs 2.5% for BPH; other procedures where patients exhibiting both prostate cancer & BPH or salvage therapy for patients undergoing alternative treatment beforehand) but we have long known that the device has been used to treat BPH before, predominantly though not exclusively at radiology centers in Germany where TULSA-PRO utility in BPH therapy was initially explored.

  - The most recent study we reviewed in the medical literature was published in Mar/25 by Germany-based Alta Klinik in the *Journal of Endourology*, showing in a 300-patient study at up to fourteen-month follow-up that even when considering patients who were ablated in the early days of TULSA-PRO roll-out, side effect profile was relatively low, with fifty-seven patients experiencing low-grade side effects that usually resolved within one month while seven patients experienced mid-level side effect severity that took a bit longer to resolve (about three months) but did indeed resolve. IPSS scores did worsen acutely but then improved to better than baseline levels at four-year follow-up. Erectile function & continence measures were generally favorable as well & presumably could improve as procedure volumes & practitioner experience improves, as we invariably see with procedure-based medical technologies.

- Profound's market value is starting to equilibrate up to levels that we believe are more justifiable for the firm at its current stage of product development, with TULSA-PRO long ago approved for all relevant prostate-specific indications & with device-specific US reimbursement codes in place since Jan/25 to facilitate TULSA-PRO adoption in all radiology or urology centers equipped with MRI functionality. During its FQ325 update, Profound held firm on its projection that at least seventy-five TULSA-PRO systems could be installed worldwide by end-of-year.

- Installed base was at seventy TULSA-PRO systems at end-of-F2025, a level that we will admit is below the level we projected a few years ago based on the impact that we thought US reimbursement codes could have on commercial adoption over a shorter launch horizon, but momentum is starting to build & we see no evidence in the medical literature, from TACT or CAPTAIN or any clinician-sponsored clinician-sponsored studies, that confer anything but positive regard for TULSA-PRO's utility in treating localized disease.

- Profound's main EU-based competitor EDAP TMS (EDAP-Q, NR) is reporting positive momentum for its own ultrasound ablation platform Focal One, generating 49% y/y revenue growth for its overall ultrasound ablation operations & 167% y/y growth in Focal One system placements worldwide along with a 15% y/y growth in procedure volumes, clearly facilitated in part by growth in system placements. Focal One has its own FDA approval & supportive clinical data, plus its own US reimbursement codes that we assume are independently driving its own unit sales in the same manner in which we expect TULSA-PRO's reimbursement-enabled system sales to grow throughout our forecast period. We are maintaining our Buy rating & PT of US$15.25 on Profound, with our valuation still based on NPV & multiples of our F2029 adjusted EBITDA/fd EPS forecast of US$69.5M & US$1.55/shr, respectively. As indicated in Exhibit 1, PRN is one of our top performers over the trailing four-week period, generating return of 16.2% over that short time frame.

Updates From Other Domestic Healthcare/Biotechnology Firms

- **Satellos peer firm Capricor Therapeutics' (CAPR-Q, NR) experiences substantial market value accretion after reporting positive phase III data for Duchenne muscular dystrophy (DMD)-targeted Deramiocel/CAP-1002 in the HOPE-3 trial.** Capricor reported positive topline data from the HOPE-3 Phase 3 trial evaluating deramiocel (allogeneic cardiosphere-derived cell therapy) in 106 patients with DMD-associated cardiomyopathy. The trial met its primary endpoint (mean change in Performance of Upper Limb (PUL 2.0) total score at 12 months), demonstrating 54% slowing of disease progression versus placebo (p=0.029), corresponding to a 1.2-point treatment difference on the 42-point scale.

  - The key secondary endpoint, left ventricular ejection fraction (LVEF), demonstrated 91% slowing of cardiac decline (p=0.041), representing a 2.4 percentage point preservation. Management clarified on the conference call that absolute value differences for both endpoints achieved statistical significance using ANCOVA baseline-adjusted analysis, consistent with a pre-specified statistical analysis plan aligned with FDA guidance. Of note, there was also observed differences in the PUL 2.0 mid-level dimension (p=0.008, 1.0-point difference). This was one of the endpoints that failed in HOPE-2 and triggered FDA's Jul/25 Complete Response Letter.

  - This marks the first time a Phase 3 DMD trial targeting cardiomyopathy has met the relevant endpoints, addressing FDA's prior objection that deramiocel lacked "substantial evidence of effectiveness". Questions still remain whether or not the primary endpoint meeting skeletal muscle outcomes will translate from a labelling perspective. HOPE-3's outcome validates mutation-agnostic strategies targeting secondary disease pathology rather than dystrophin restoration.

  - Deramiocel's cell-therapy MOA is claimed to address downstream inflammation and fibrosis without requiring dystrophin expression & these data support the claim that demonstrating that skeletal and cardiac functional preservation is achievable through alternative mechanisms. This holds positive de-risking in the clinical and regulatory pathway for other dystrophin-independent approaches in DMD, relevant to ON-based Satellos Biosciences (MSCL-TSX, NR) & its small-molecule AAK1-inhibiting SAT-3247, on which we have frequently commented in prior Healthcare Weeklies & for which positive if limited preclinical & Phase II efficacy data are already in the public domain.

- **Cleveland Diagnostics received FDA approval for novel prostate cancer diagnostic assay.** OH-based private diagnostic test developer Cleveland Diagnostics received FDA approval this week for IsoPSA, its laboratory-developed CLIA-certified assay for prostate cancer. IsoPSA is based on the firm's IsoClear protein biomarker platform that has the ability to assess structural changes in proteins that may themselves be diagnostic of disease, independent of quantification of a protein biomarker that

may also be diagnostic of disease if its expression is above a defined threshold. Structural changes in PSA can influence where it can be found in the body (in serum or in the prostate gland itself, the two major tissues where it could be found).

- Unlike standard serum PSA tests, the IsoPSA test infers structural changes in PSA by calculating the ratio of total & free PSA Cleveland & its collaborators published an IsoPSA study in Jul/25 in the *Journal of Urology*, in which a survey of 1,578 patients were stratified by levels of serum PSA at enrollment & then determined to have either a low (less than 6) or high (above 6) IsoPSA index. Patients were then assessed either with prostate MRI or with prostate biopsy to confirm prostate cancer diagnosis or lack thereof to see if legacy methods were correlate with IsoPSA index.

- It turned out that the correlation was quite strong, with low IsoPSA patients exhibiting a risk of developing clinically-significant prostate cancer at one-, two- or three-year follow-up was 0.4%-2.5%-6.3% respectively, while the risk at equivalent timepoints for high IsoPSA patients was far higher at 5.9%-31.7%-49.5%. These data were qualitatively similar if quantitatively distinct from a 2023 study (using the same IsoPSA threshold of 6 for discriminating between low & high patients) that was published in abstract form at the 2023 ASCO meeting. The IsoPSA blood test has in fact been marketed since 2020 following its Breakthrough Device Designation from the FDA in F2019 & has been partnered with Quest Diagnostics (DGX-NY, NR) since Feb/23

- The test will compete in a prostate cancer diagnostics market that does have a few competitors already, including SelectMDx Test developed by Belgium-based MDxHealth SA (MDXH-Q, NR) & its ExoDx Prostate Test that it acquired from MN-based Bio-Techne (TECH-Q, NR) in Aug/25, as well as OPKO Health's (OPK-Q, NR) 4Kscore Test that was just FDA-approved itself in Jul/25 & MI-based Lynx Dx's (private) urine-based MyProstateScore 2.0 (MPS2) multiplexed biomarker test (the main gene transcript it identifies is the fusion protein T2:ERG, encoded by a gene that is a fusion of the transmembrane protease serine 2 [*TMPRSS2]* gene & the erythroblastosis virus E26 oncogene homolog [*ERG]* genes). We reflect with some sadness that DiagnoCure's (ticker was CUR-T, a former coverage stock of ours) urine-based non-coding mRNA-PCA3 diagnostic assay (Progensa), that was partnered with Gen-Probe (acquired by Hologic [HOLX-Q, NR] in Aug/12) & was itself FDA-approved back in Feb/12 based on data from 509-patient study completed in F2010, was never able to generate any commercial traction.

- But at present, we are tracking advances in cancer diagnosis through our interests in telomere architecture analysis firm Telo Genomics (TELO-V, NR) & its TeloView platform. The firm is already collaborating with the US-based Mayo Clinic to test TeloView's utility in diagnosing/staging multiple myeloma, with encouraging data in smoldering multiple myeloma already published in May/24 in the *American Journal of Haematology* & with a new 70-patient clinical program in collaboration with the US-based Cleveland Clinic & McGill University assessing TeloView utility in diagnosing measurable residual disease (MRD) in multiple myeloma for which interim data were reported at the 2025 ASCO meeting (final data expected by late F2027).

- In Telo's product pipeline, it identifies prostate cancer (& interestingly, Alzheimer's disease on which we commented above in regard to pTau181/pTau217 blood-based analysis) as one of its target indications & at initial inspection, this seems like a plausible secondary market to pursue after multiple myeloma, for which its clinical programs are both partnered & well-advanced already. Telo's scientific founder Sabine Mai has indeed published prostate cancer-relevant TeloView telomere architecture data in recent years, including but not limited to a 2020 study in the journal *Cells* & a separate 2019 study in the journal *Cancers*, among other earlier publications.

Potpourri Of Other Healthcare/Biotechnology Updates

- **Imvax (Private) reports 6.3-month overall survival benefit in its Phase IIb newly diagnosed glioblastoma trial, FDA meeting to discuss next-steps is imminent.** Topline results were announced from its randomized, double-blind, placebo-controlled Phase IIb trial evaluating IGV-001 in 99 newly diagnosed glioblastoma (ndGBM) patients. The trial enrolled patients in a 2:1 randomization across 19 U.S. sites, with patients receiving either bio-diffusion chambers containing personalized whole tumor-derived cells with an antisense oligonucleotide (IGV-001 arm) or inactive solution (placebo arm) approximately 48 hours post-surgical resection. While the trial missed its primary endpoint of progression-free survival (PFS), the IGV-001 arm demonstrated a median overall survival (mOS) of 20.3 months compared to 14.0 months in the placebo arm, representing a 6.3-month (45%) improvement with median follow-up of 22 months. The company has informed the FDA it intends to request a meeting to discuss the regulatory pathway, likely pursuing accelerated approval despite a PFS miss.

- IGV-001 is an autologous, whole-tumor–derived immunotherapy that uses a small sample of the patient's own tumor tissue harvested during surgical resection. The tumor cells are treated and briefly implanted in a sealed bio-diffusion device at an abdominal site for approximately 48 hours before being removed. This ex vivo process is designed to induce immunogenic cell death, which releases tumor antigens and danger signals that train the immune system to recognize and attack residual glioblastoma cells throughout the body.

- The trial missed its primary endpoint of PFS, which warrants closer examination of what PFS measures in practice. PFS is essentially a binary assessment of time-to-progression based on imaging criteria and may not fully capture differences in tumor growth velocity or kinetics. If the therapy is slowing progression without cleanly preventing it according to standard radiographic thresholds, this could fail to register as a PFS benefit while still extending OS. Research published by Prasad and colleagues in *JAMA Internal Medicine* examined 65 trial-level correlations between surrogate endpoints (like PFS) and OS in oncology, finding that 52% showed low correlation and only 23% showed high correlation, with separate analyses demonstrating that OS benefit without PFS benefit occurs in approximately 31% of oncology trials.

- The 6.3-month improvement in median OS suggests some underlying biological effect is at work, and if the company can demonstrate that slower tumor kinetics, delayed symptomatic progression, or other measurable factors are driving this survival benefit, it would strengthen the case that a clinically meaningful mechanism is operating even when the traditional PFS endpoint doesn't capture it. Notably, Prasad now serves as director of the FDA's Center for Biologics Evaluation and Research, which oversees biologic-device combinations, potentially creating a regulatory environment more receptive to OS-driven benefit arguments in cases where PFS and OS diverge.

- **Final FDA minutes from uniQure's (QURE-Q, NR) pre-BLA meeting for AMT-130 Huntington's Gene Therapy confirms their phase I/II data will not be sufficient.** The FDA indicated that data compared to external controls "are currently unlikely to provide the primary evidence to support a BLA submission" and uniQure plans to request a follow-up meeting in Q1 2026 to discuss alternative regulatory pathways. The feedback is particularly notable in light of the FDA's September 2025 draft guidance on cell and gene therapies for small populations, which explicitly lists externally controlled studies as a potentially acceptable trial design for gene therapies in settings where traditional randomized trials are challenging. In parallel, FDA leadership, including Commissioner Makary and CBER Director Prasad, have highlighted more flexible approaches for gene therapies in a November 2025 NEJM piece describing a "plausible mechanism" pathway for certain personalized or bespoke interventions.

  - Taken together, the AMT-130 feedback suggests some dissonance between higher-level guidance statements and case-by-case review standards, or alternatively that uniQure's specific external control methodology, endpoints, or data robustness did not meet the bar. In the latter case, disconnect could stem from multiple speculative factors: inadequate matching of external controls to the treatment population, insufficient statistical power or pre-specification of analyses, concerns about the durability or clinical meaningfulness of observed effects, or issues with the selected endpoints themselves that may not align with what the FDA now views as approvable evidence for this indication.

- **FDA approves pirtobrutinib for treating chronic lymphocytic leukemia/small lymphocytic lymphoma**. Earlier this week, the US FDA expanded the suite of approved leukemia/lymphoma indications for Eli Lilly's (LLY-NY, NR) BTK inhibitor small-molecule drug pirtobrutinib/Jaypirca. Full traditional approval was officially granted in this announcement after the drug garnered accelerated approval back in 2023 for treating patients who has already become refractory to at least one other BTK inhibitor drug (of which there are a few, the most prominent of which is Janssen/Pharmacyclics' ibrutinib/Imbruvica, & a BCL-2 inhibitor drug (probably AbbVie's [ABBV-NY, NR] venetoclax/Venclexta).

  - The approval was based on data from Eli Lilly's 238-patient BRUIN-CLL-321 trial in which previously-treated chronic lymphocytic leukemia or small lymphocytic lymphoma patients exhibited progression-free survival of 11.2 months in comparison to 8.7 months for patients treated with control therapy (some combination of Roche/Genentech's [ROG-SW, NR] CD20-targeted rituximab/Rituxan, Cephalon's [private] small-molecule DNA alkylating drug bendamustine/Treanda or Gilead's [GILD-Q, NR] phosphatidylinositol 3-kinase delta inhibitor iselalisib/Zydelig). Median duration of follow-up was only 19.8 months at the time of approval & so overall survival benefit was not yet established.

  - In a separate announcement from Eli Lilly, the firm announced that data from two other pirtobrutinib-based chronic lymphocytic leukemia studies ae poised to be presented at the annual American Society of Haematology (ASH) meeting, including from the BRUIN CLL-313 (testing pirtobrutinib in treatment-naïve CLL patients as a first-line therapy in patients

without a deletion in the 17p region of chromosome 17, as is frequently found in CLL patients) & the BRUIN-CLL-314 (pirtobrutinib will be compare directly to the aforementioned ibrutinib/Imbruvica) trials.

- While it seems plausible to assume that much of Eli Lilly's market value ascent in recent trading sessions is being driven by its diabetes/endocrinology franchise – long-acting GLP-1 analog drugs Mounjaro & Zepbound (different formulations of tirzepatide) collectively generated US$10.1B of the firm's US$17.6B in total product revenue in FQ325 – Jaypirca's FQ325 sales were still US$143M & thus solid in absolute terms if not at the top end of Eli Lilly's commercial Rx portfolio. Moreover, it is featured quite prominently in Eli Lilly's clinical pipeline & pending milestones as described in the firm's FQ324 investor presentation.

Capital Markets Summary

Exhibit 5. EBITDA Or EPS-Positive Canadian Healthcare Stocks

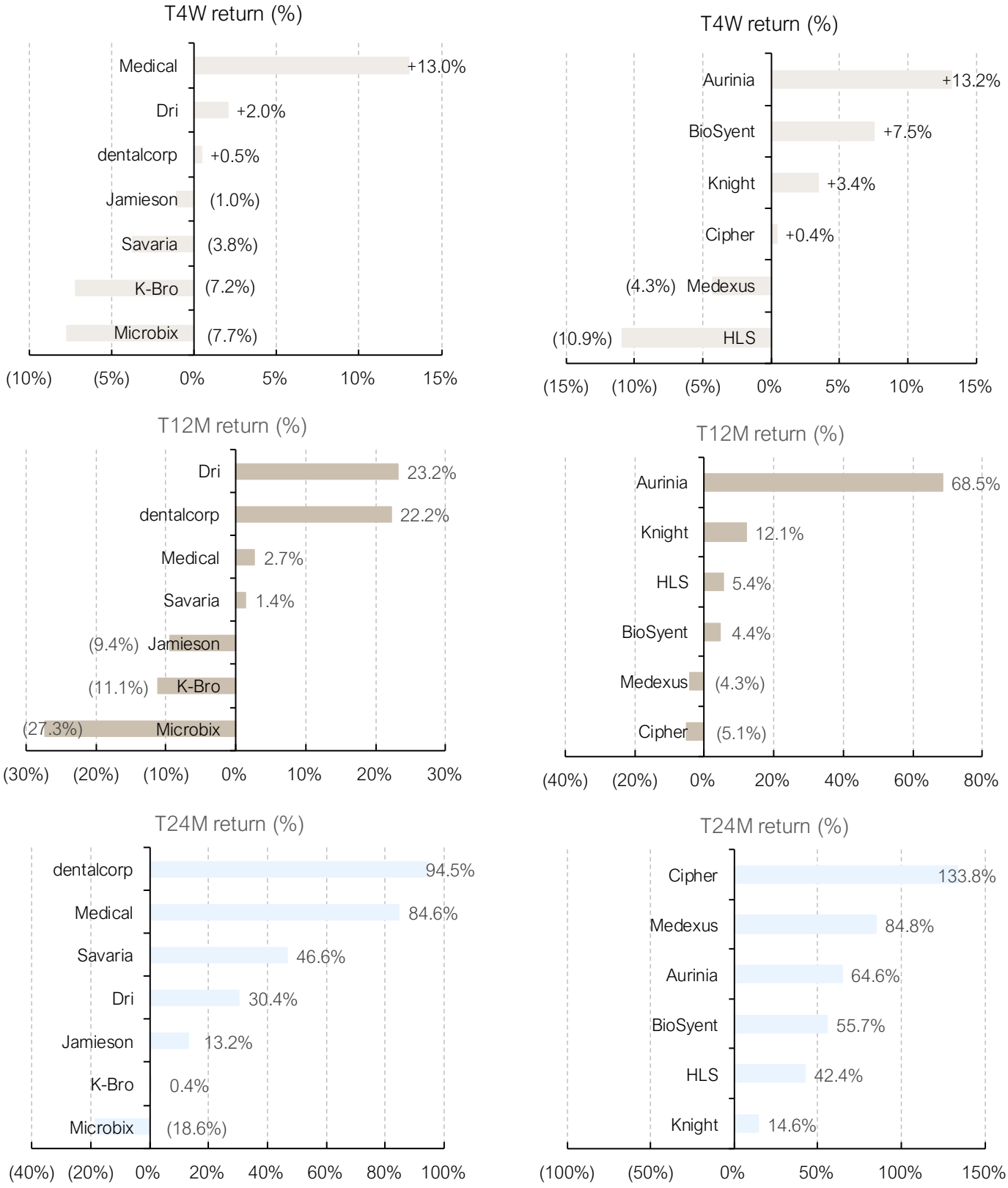
Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 03-Dec	Mkt Cap (M)	Mkt Cap (C$M)	Ent. Value (M)	Ent. Value (C$M)	EV/EBITDA (T12M)	EV/EBITDA FY1	EV/EBITDA FY2	Price/Earnings (T12M)	Price/Earnings FY1	Price/Earnings FY2
Profitable Canadian healthcare firms - specialty services [2]														
dentalcorp Holdings	CAD	DNTL	191.3	$10.95	2,095	2,095	3,425	3,425	12.0x	10.7x	9.6x	NA	20.6x	18.9x
DRI Healthcare Trust	CAD	DHT.UN	55.1	$16.51	910	910	1,324	1,324	8.6x	5.8x	5.8x	NA	8.0x	7.2x
Jamieson Wellness	CAD	JWEL	41.9	$34.14	1,430	1,430	1,867	1,867	13.0x	11.7x	10.3x	22.9x	18.3x	14.9x
K-Bro Linen	CAD	KBL	13.0	$34.98	454	454	755	755	8.5x	7.8x	7.0x	21.0x	17.7x	15.2x
Medical Facilities [1]	CAD	DR	18.1	$11.70	211	295	402	561	7.1x	5.5x	5.6x	7.6x	9.5x	9.8x
Microbix Biosystems	CAD	MBX	139.0	$0.24	33	33	28	28	11.5x	NA	NA	NA	NA	NA
Savaria	CAD	SIS	71.6	$21.30	1,525	1,525	1,749	1,749	NA	9.7x	8.7x	31.2x	18.2x	15.8x
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales [2]														
Aurinia Pharmaceuticals	USD	AUPH	131.8	$14.91	1,966	2,742	1,686	2,352	11.4x	9.7x	8.3x	25.8x	19.4x	15.9x
Bausch Health	USD	BHC	370.9	$7.05	2,615	3,647	32,462	45,285	9.9x	9.0x	8.7x	7.2x	1.8x	1.7x
BioSyent	CAD	RX	11.5	$11.83	136	136	113	113	7.9x	9.1x	9.0x	15.5x	16.0x	13.6x
Cipher Pharmaceuticals [1]	CAD	CPH	25.4	$10.61	269	375	382	533	19.4x	14.5x	14.2x	15.7x	15.4x	17.3x
HLS Therapeutics	CAD	HLS	31.3	$4.90	153	153	213	213	9.6x	7.8x	6.8x	NA	NA	NA
Knight Therapeutics	CAD	GUD	99.3	$6.04	600	600	587	587	11.4x	9.7x	9.1x	NA	NA	NA
Medexus Pharmaceuticals	CAD	MDP	32.4	$2.68	87	87	103	103	4.9x	3.6x	5.7x	NA	49.1x	NA
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales														
CareRx	CAD	CRRX	62.8	$3.47	218	218	284	284	10.2x	8.6x	7.3x	NA	49.2x	17.4x
Chartwell Retirement Residences	CAD	CSH.UN	303.9	$20.00	6,079	6,079	8,655	8,655	23.2x	21.6x	17.7x	NA	NA	NA
Extendicare	CAD	EXE	83.8	$20.99	1,759	1,759	1,929	1,929	11.6x	11.4x	8.9x	19.5x	19.9x	17.9x
Northwest Healthcare Properties REIT	CAD	NWH.UN	250.0	$5.39	1,347	1,347	5,200	5,200	20.1x	21.4x	21.7x	26.9x	NA	NA
Nova Leap Health	CAD	NLH	87.3	$0.34	30	30	32	32	12.3x	NA	NA	39.1x	NA	NA
Sienna Senior Living	CAD	SIA	94.1	$20.52	1,931	1,931	3,157	3,157	22.1x	19.6x	16.1x	45.7x	42.8x	35.4x
Profitable Canadian healthcare firms - medical equipment distribution/sales														
Covalon Technologies	CAD	COV	27.6	$1.95	54	54	37	37	11.8x	21.6x	7.7x	22.6x	NA	16.3x
Quipt Home Medical	USD	QIPT	43.4	$2.42	105	147	259	361	NA	4.8x	4.0x	NA	NA	NA
Viemed Healthcare	USD	VMD	38.0	$6.76	257	257	375	523	8.4x	6.5x	5.8x	19.4x	18.5x	13.3x
Profitable Canadian healthcare firms - medical equipment distribution/sales														
Healwell AI	CAD	AIDX	280.9	$0.93	261	261	338	338	NA	NA	31.4x	NA	NA	NA
Kneat.com	CAD	KSI	95.3	$4.67	445	621	415	415	NA	44.6x	25.1x	NA	NA	NA
Vitalhub	CAD	VHI	63.1	$9.36	591	824	468	468	21.4x	18.3x	13.7x	NA	NA	34.0x
Well Health Technologies	CAD	WELL	253.9	$4.00	1,016	1,016	1,711	1,711	16.5x	8.6x	8.2x	NA	9.6x	9.8x
Average									**12.7x**	**12.6x**	**11.1x**	**22.9x**	**20.9x**	**16.1x**
Recently-acquired Canadian healthcare firms														
Andlauer	*CAD*	*AND*	*39.2*	*$54.97*	*2,152*	*2,152*	*2,165*	*2,165*	*13.4x*	*NA*	*NA*	*32.0x*	*NA*	*NA*
Theratechnologies	*CAD*	*TH*	*46.0*	*$4.47*	*206*	*206*	*238*	*238*	*12.3x*	*NA*	*NA*	*NA*	*NA*	*NA*

[1] Share price converted to USD for stocks reporting financial data in USD but for which share value is reported in CAD; price refers to prior day close, EV calculations based on cash/LT debt reported in most recent quarter

[2] Legacy specialty pharmaceutical firm & coverage stock Theratechnologies (TH-T, THTX-Q) was acquired in Sept/25 by CB Biotechnology/Future Pak for cumulative consideration of US$4.20/shr; Andlauer's acquisition by UPS (UPS-NY, NR) is now closed as of Nov/25

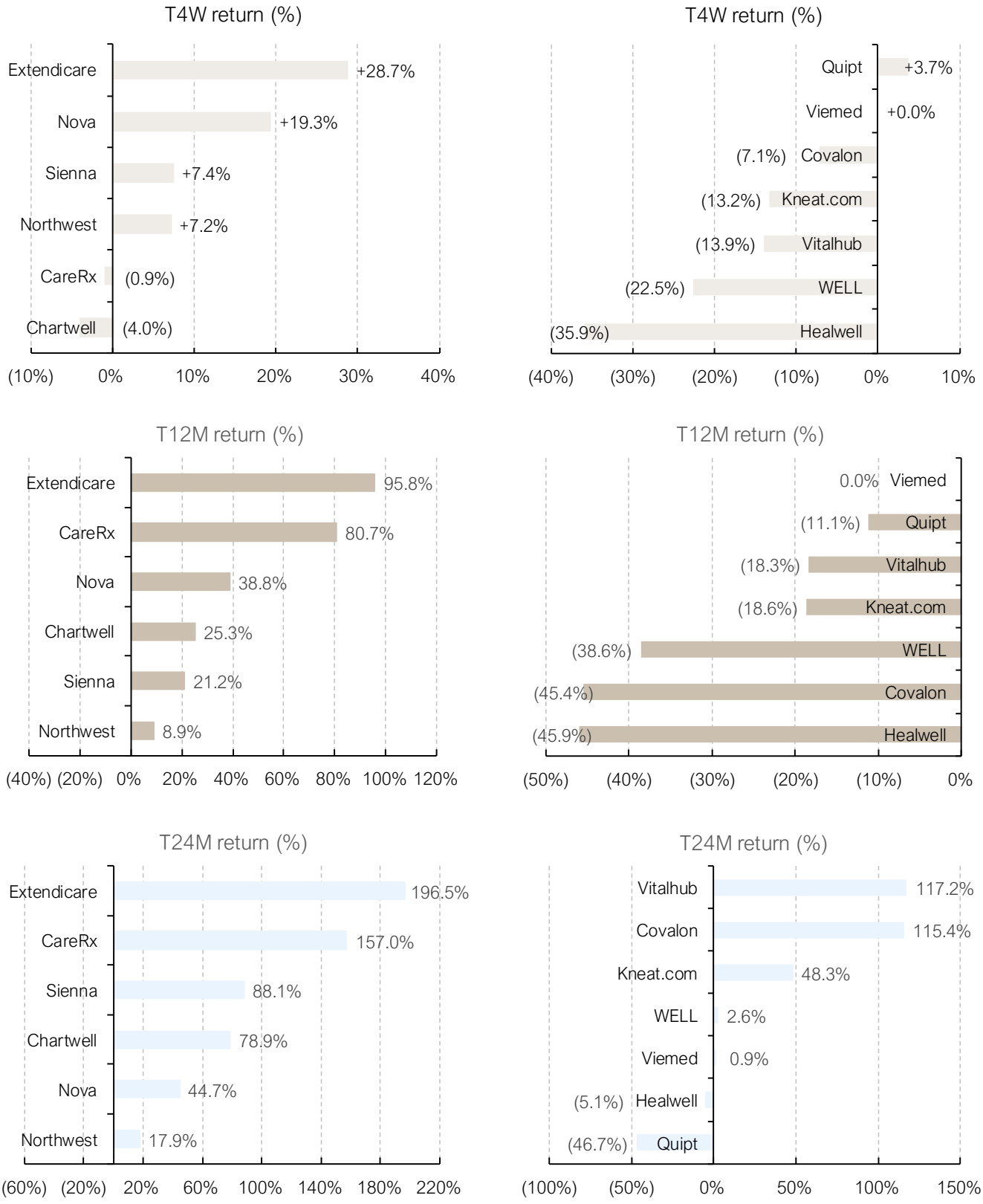
Source: Refinitiv, company reports, Leede Financial

Exhibit 6. Trailing Four-Week, One-Year & Two-Year Relative Share Price Performance For EBITDA/EPS-Positive Canadian Healthcare Equities – Specialty Services & Specialty Pharmaceutical Firms



Source: Refinitiv, company reports, Leede Financial

Exhibit 7. Trailing Four-Week, One-Year & Two-Year Relative Share Price Performance For EBITDA/EPS-Positive Canadian Healthcare Equities – Eldercare Services & Medical Technology Distribution/Healthcare IT Services



Source: Refinitiv, company reports, Leede Financial

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RECOMMENDATION	NO. OF COMPANIES	%
Buy	7	41%
Speculative Buy	7	41%
Hold	2	12%
Sell	-	-
Tender	1	6%
Under Review	-	-

Historical Target Price

Appili Therapeutics | APLI-TSXV	None
Cardiol Therapeutics | CRDL-TSX, NASDAQ	None
CareRx | CRRX-TSX	None
Cipher Pharmaceuticals | CPH-TSX	None
Eupraxia Pharmaceuticals | EPRX-TSX, NASDAQ	None
Extendicare | EXE-TSX	None
K-Bro Linen | KBL-TSX	4,5
Medexus Pharmaceuticals | MDP-TSX	4
Medical Facilities | DR-TSX	None
Nanalysis Scientific | NSCI-TSXV	None
Oncolytics Biotech | ONCY-NASDAQ	None
Perimeter Medical Imaging | PINK-TSXV	None
Profound Medical | PRN-TSX, PROF-NASDAQ	None
ProMIS Neurosciences | PMN-NASDAQ	2
Quipt Home Medical | QIPT-TSX, NASDAQ	None
Sernova Biotechnologies | SVA-TSX	2