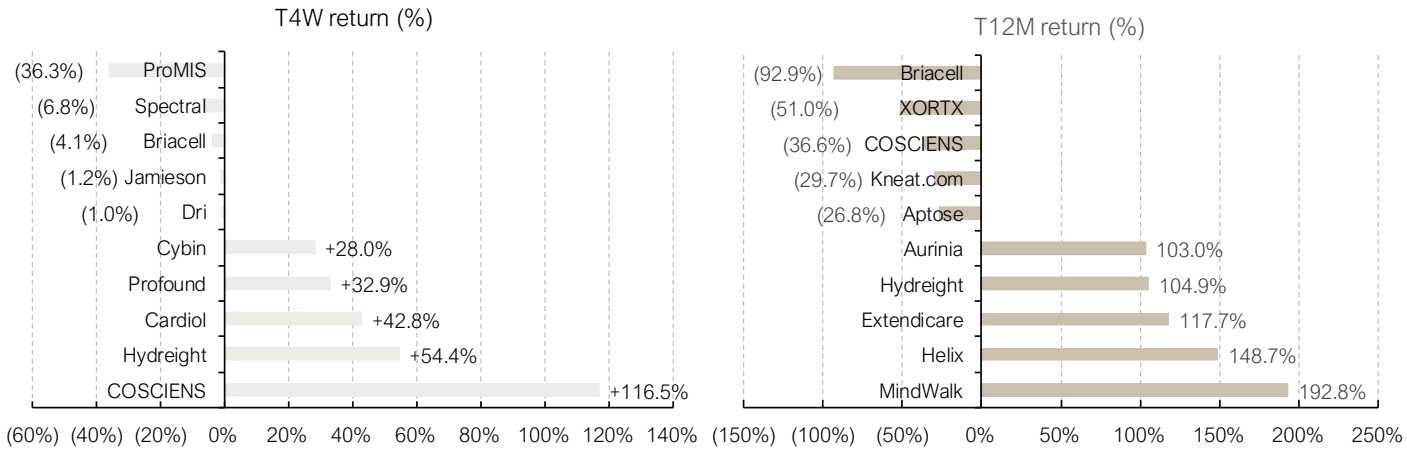
Core Highlights of the Week

Top Movers

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



Source: Leede Financial, Refinitiv

Updates From Our Healthcare Universe

- **Eupraxia's Phase II eosinophilic esophagitis (EoE)-targeted RESOLVE trial generates impressive tissue normalization at nine-month follow-up in its high-dose/high-injection volume Cohort 9 - sharpens catalyst map and pipeline guidance.** BC-based inflammatory disease-focused drug delivery innovator Eupraxia Pharmaceuticals (EPRX-Q, Buy, PT US$12.75) reported first 36-week (nine-month) tissue health and symptom data from three patients enrolled in one of its focus patient cohorts (so-called Cohort 9; twenty injections of the firm's DiffuSphere-based fluticasone propionate formulation EP-104GI at 8-mg per injection), which is the highest dose being tested in the open-label, dose-escalation Phase Ib/IIa portion of the 117-patient RESOLVE trial.

  - Changes in esophagus tissue histology as measured by the EoE histology scoring system (EoEHSS) showed a stage reduction of 0.59 under the criteria defined by HSS (-90%) and grade reduction of 0.53 (-88%) at week 36, both of which were the deepest levels observed across all cohorts at this timepoint, with improvements based both on mitigating levels of pro-inflammatory markers (notably eosinophil infiltration) & tissue structure/architectural sub-scores. Peak eosinophil count (PEC) fell 72% from baseline, also the largest reduction across all cohorts tested so far.

  - Mean impact on the Straumann Dysphagia Index (SDI) declined 3.0 points at week 36 (this is a pre-specified clinical remission threshold), with two of three patients (66%) maintaining remission from week 8 through week 36. Safety remains clean across all 31 treated patients and >230 patient-months of follow-up: no drug-related SAEs, no oropharyngeal candidiasis, and no adrenal insufficiency or glucose derangement, including in one patient with type 2 diabetes.

  - 36-week data, especially new Cohort 9 data, remain a solid confirmation of EP104GI's durability in our view. Absolute histology and SDI values show clinically-meaningful symptom stability as compared to six-month data previously

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reported (mean SDI improvement moderating from roughly -4 to -3 points; EoEHSS grade/stage from approximately -0.63/-0.57 to -0.53/-0.59), consistent with normal biological variability in a three-patient cohort being followed toward the outer edge of the intended dosing interval. The proportion of patients in SDI remission is unchanged at 66%, which in our view is the more interpretively durable metric than point-in-time absolute means.

- As we noted in our last EPRX report, what matters at this stage of dose escalation in our view is whether the efficacy signal holds together across multiple measures, including all of the various endpoints (EoEHHS, SDI), all of the various cohorts & during the time that local fluticasone propionate dosing intensity rises as drug diffuses away from DiffuSphere & into diseased tissue.

- Histology continues to compare well with other FDA-approved EoE therapies, with our usual qualifier that comparing data across different trials that have not been similarly randomized can introduce confounding variables & thus confounding analysis. But that aside, we of course compare data in distinct trials all the time & will do so in this circumstance as well, qualifiers notwithstanding. For example, in the placebo-controlled LIBERTY EoE TREET, dupilumab 300mg weekly generated LS mean EoEHSS grade and stage reductions of approximately 62% and 60% at week 24, with architectural subscores of 50% and 46% (Collins, Gastro Hep Advances, 2025), sustained on continuous biweekly dosing thereafter. Cohort 9 is now showing 88% and 90% reductions in grade and stage at week 36 from a single administration; not a head-to-head claim, but a directional comparison that continues to hold.

- We expect quarterly Phase Ib/IIa readouts through Q3 2026, topline Phase IIb RESOLVE data in Q4 2026, an End-of-Phase II FDA meeting in H1 2027, and initiation of a single 150–300-patient, 52-week registrational Phase III in mid-2027. Approximate cash on hand of US$140M provides funds for EP104GI clinical activities well into H228, including for funding Phase IIb EoE testing to final data & to commence pivotal Phase III EoE testing without the need to augment existing cash balance or to solicit partnership interest, at least not yet. Separately, Eupraxia has explicitly identified a timeline for their new GI indications in H2 2026, with benign esophageal strictures and fibrostenosing Crohn's disease named as the leading candidates, a meaningful step beyond the MD&A language we flagged in March, which framed those indications as plausible but not yet scheduled. Our model continues to ascribe no value to secondary indications pending a formal clinical and regulatory path. The Phase III sizing at 150–300 patients for a single pivotal trial is consistent with our existing assumptions. Net-net, incrementally positive; the Phase IIb Q4 2026 topline remains the important catalyst.

Other Significant Clinical Trial Updates With Relevance To Our Coverage Universe

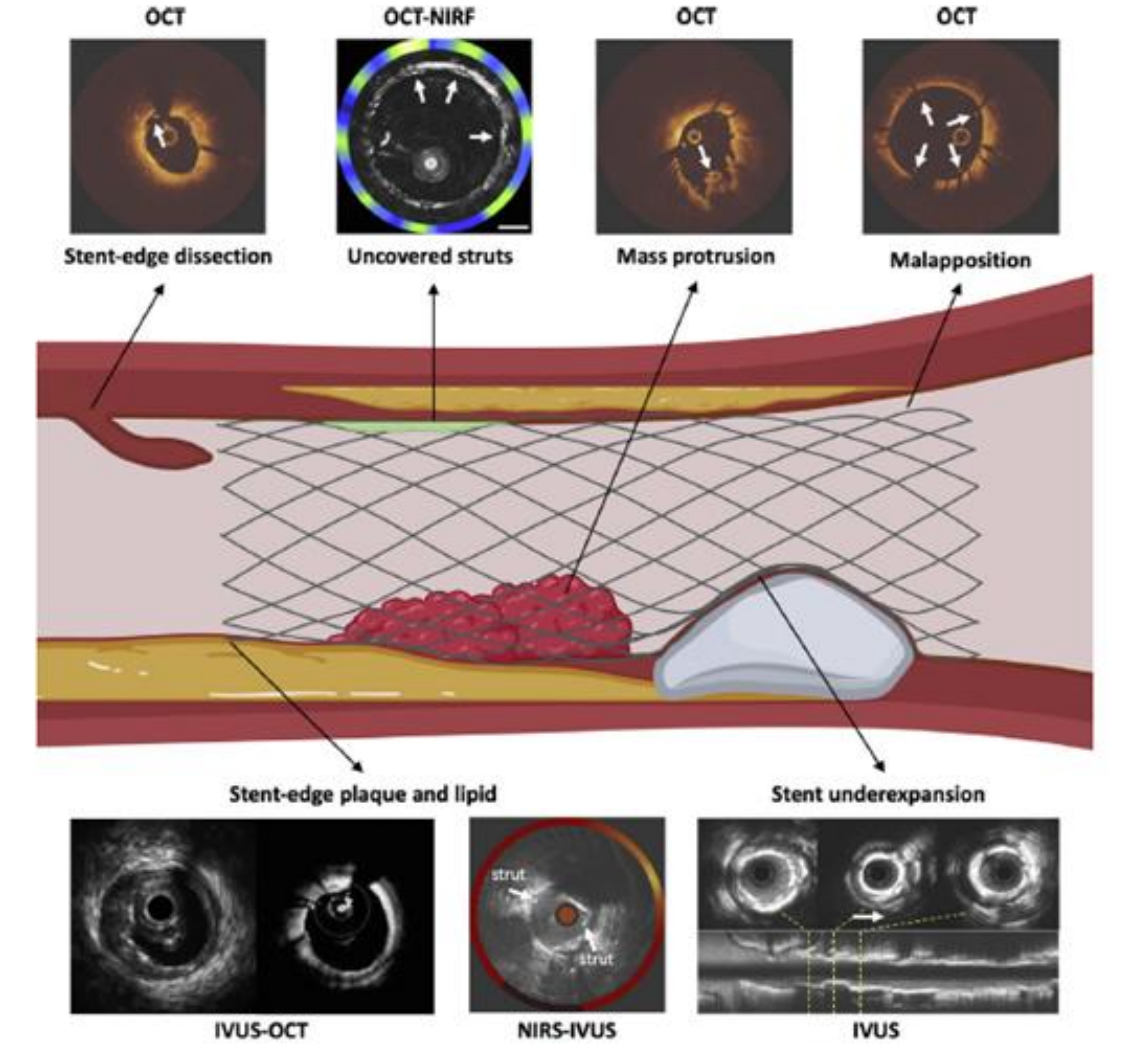
- **Conavi receives FDA approval for its hybrid IVUS-OCT intravascular imaging platform.** ON-based medical technology developer Conavi Medical (CNVI-V, NR) just received US FDA approval via the 510(k) regulatory review process for its intravascular ultrasound (IVUS) & optical coherence tomography (OCT)-based intravascular imaging catheter platform. Like previous incarnations of Conavi's hybrid IVUS-OCT imaging catheter platform, we assume that the target market is interventional cardiology, whereby the device would be used to accurately assess deployment of blood vessel-stabilizing stents for patients undergoing balloon angioplasty procedures.

  - Interestingly, Conavi does not identify a brand for the newly-FDA-approved hybrid catheter platform even though earlier-generation variants of the technology were branded as Novasight Hybrid System. We expect this to be a trivial detail in the device's pace of adoption in US interventional cardiology markets but it is plausible that novel branding initiatives could be on the horizon.

  - We have visited Conavi either at its corporate offices in Toronto or at Sunnybrook Hospital from which the foundational technology emanates & hold the hybrid imaging platform in high regard, both for device-specific & medical market-specific reasons. The medical justification for assessing vascular integrity both pre- & post-vascular intervention of some type is widely recognized & the utility of combining ultrasound-based imaging with some sort of visual light-based imaging modality is equally well-recognized in the medical literature.

  - We have cited the figure featured in Exhibit 2 before in our Healthcare Weekly, but it bears reflection in the wake of Conavi's 510(k) approval just announced (we see that Conavi itself reproduces this figure in its own investor presentation) – as shown, the combination of intravascular ultrasound & optical coherence tomography provides the greatest capability for identifying failures in stent deployment & we thus see no technical impediments to its broader adoption in the US interventional cardiology market over time.

Exhibit 2. Performance Of Standalone & Hybrid Intravascular Imaging In Detecting The Most Common Causes Of Stent Failure



Imaging modality	Stent underexpansion	Stent-edge plaque	Stent-edge lipid	Stent-edge dissection	Mass protrusion	Malapposition	Uncovered struts
IVUS							
OCT							
IVUS-OCT							
NIRS-IVUS							
OCT-NIRS							
NIRF-IVUS							
OCT-NIRF							
FLIm-IVUS							
FLIm-OCT							
IVPA-IVUS							

Source: *JACC : Cardiovascular Interventions (2024). Vol. 17, pp. 1963-1979*

- Earlier this year, Conavi & collaborators published a plaque visualization study in the journal *Cardiovascular Research*, nicely showing that hybrid IVUS-OCT plaque analysis was superior for identifying plaque components associated with fibrotic or calcified or necrotic components, any one of which can lead to more substantive vessel blockage over time. And as Exhibit 3 shows (originally published in 2022 in *JACC: Cardiovascular Imaging),* IVUS & OCT do have their own

limitations but which in most cases can be offset through the complementary image contrast characteristics that are intrinsic to the respective platforms.

- Detection of vulnerable plaque is of growing interest in interventional cardiology based more on the growing awareness of plaque architecture in predicting more extensive vascular disease & independent of the emergence of IVUS-OCT specifically, But in the 2024 *JACC: Cardiovascular Imaging* paper from which we cite Exhibit 2, it appears that IVUS-OCT in combination are superior to most other modalities at identifying regions of calcification within intravascular plaque, a key metric for determining cardiovascular risk.

Exhibit 3. Specific Situations In Which IVUS Is Preferred Over OCT Or Vice Versa, Thus Supporting The Concept Of Combining The Two Modalities In A Single Device, Which Conavi Has Accomplished

Situation	Preferred Device	Reason
Culprit in acute coronary syndrome	OCT	OCT can detect & differentiate red from white thrombus & identify erosions
Suspected spontaneous coronary artery dissection	IVUS	Flushing needed during OCT may propagate the dissection
Aorto-ostial lesions	IVUS	Clearing blood from the aorto-ostial junction is problematic
Left main coronary artery percutaneous coronary intervention (LMCA-PCI)	IVUS	Very little data with OCT & OCT assess-ment of the aorto-osteal junction is difficult
Chronic total occlusion	IVUS	Flushing needed during OCT may propagate the dissection
Stent failure	OCT	OCT can assess stent strut covrae & detect neoatherosclerosis
Chronic renal insufficiency	IVUS	Contrast used for flushing during OCT can exacerbate renal insufficiency

Source: *JACC: Cardiovascular Imaging (2022). Vol. 15, pp. 1799-1820*

- We have long believed that intravascular imaging was a key procedure to incorporate into standard-of-care for mitigating vascular disease, if only as a way to verify extent of coronary artery or peripheral artery blockage & to ensure accurate deployment of vessel structure-stabilizing stents, but this notion came to us over twenty-five years ago, back when we were tracking market adoption of Boston Scientific/Angiotech's (BSX-NY, NR) paclitaxel-coated TAXUS stents & Johnson & Johnson's (JNJ-NY, NR) sirolimus-coated CYPHER stents, without much update of any imaging technology available at the time (including IVUS & OCT, just without being combined in one imaging catheter as Conavi has accomplished). Accordingly, we will be interested to see if IVUS-OCT combination imaging is the technical achievement that drives vascular imaging forward as a medical imperative instead of the medical idiosyncrasy that it has been until now. We see no medical impediments to adoption; commercial or reimbursement impediments may be more relevant to adoption at least in the near-term.

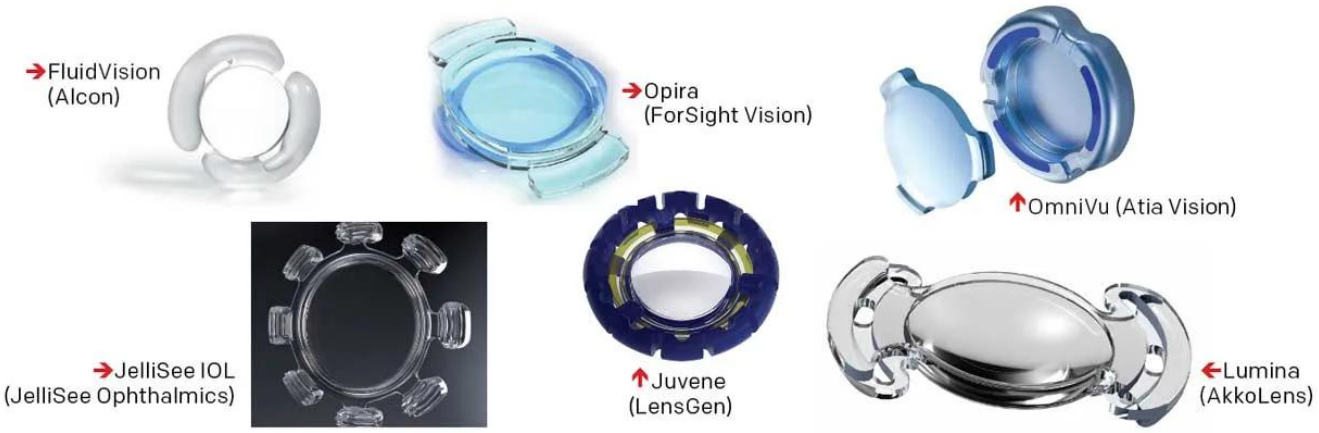
- **Ocumetics updates patient outcomes for its intraocular lens clinical program, with sustained improvements reported post-lens implantation.** We have commented on AB-based intraocular lens developer Ocumetics (OTC-V, NR) & its novel design for an accommodating intraocular lens, a device for which the first cohort of a thirty-patient first-in-human post-cataract surgery study is ongoing & already generating impressive results.

  - In our last update, we spoke to how the first patient enrolled in the trial was responding (quite favorably on improvements in visual acuity, with a documented ability to accommodate different focal planes based on whether or not the lens was required to focus on near or far objects) & in Ocumetics' most recent update earlier this week, the firm reported that at six-month follow-up, the patient was still able to sustain improved visual acuity, though Ocumetics did not quantify the magnitude of the improvement either from baseline or from the three-month follow-up previously provided.

  - Regardless, we assume that the firm will now more aggressively enroll post-cataract surgery patients to expand its suite of clinical efficacy case histories in the service of preparing for a pivotal PMA study, possibly as early as next year if this thirty-patient trial can conclude by FH127, an aggressive milestone based on pace of enrollment so far, but certainly achievable even without expanding the number of enrolling centers beyond those already in place.

- We do not formally cover Ocumetics but the firm is competing in a largely untapped intraocular lens landscape but one where some valuation metrics based on acquisition of peers are available for review. Relevant transactions include Alcon's (ALC-SW, NR) acquisition in Mar/19 of TX-based FluidVision AIOL developer PowerVision for US$285M (excluding US$135M in development/commercial milestones embedded into total deal value) & before that, Abbott Medical Optics' (ABT-NY, NR) acquisition in Sept/09 of CA-based Synchrony Dual Optic IOL developer Visiogen for US$400M. We believe that Alcon continues to compete in this industry with FluidVision AIOL-derived lenses (it performed well in a 27-patient pilot study as well as in the pivotal ORION study, as summarized in a Sept/25 issue of *Ophthalmology Management* that we reviewed) but it is likely that Visiogen's IOL was discontinued (a 410-patient lens implantation study is identified in the US NIH's clinical database as being not just completed but actually terminated as of Sept/13; still, the valuation ascribed to Abbott Medical Optics' assessment of its achievable market share in the IOL universe is obviously locked in time & unchanged).

Exhibit 4. Various Intraocular Lens Designs That Are Either Clinical- Or Commercial-Stage Devices For Which The Target Market Is Visual Acuity Improvement Post-Cataract Surgery



Source: *Ophthalmology Management (Sept/25)*

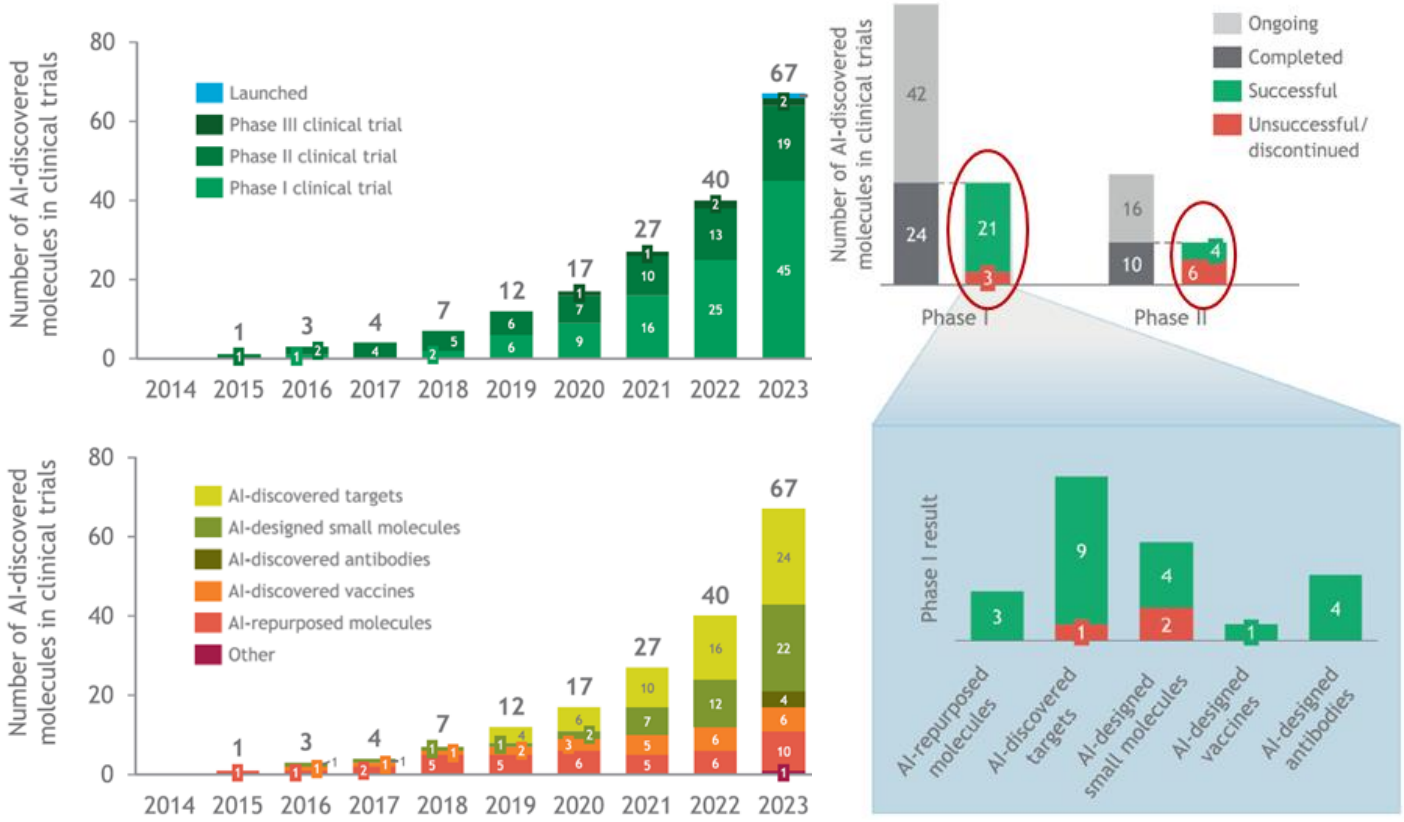
- Ocumetics does have a few competitive intra-ocular lenses that are either already approved or in active clinical testing, with the most recent FDA approval pertaining to Johnson & Johnson's (JNJ-NY, NR) TECNIS PureSee intraocular lens as announced in mid-Mar/26. But other clinical-stage lenses that by being clinical-stage are either at a comparable or more advanced stage of development to Ocumetics' IOL includes:
  - Juvene lens developed by CA-based private firm LensGen (a 51-patient visual acuity trial concluded in 2020 & was published in Oct/22 in the *Journal of Cataract & Refractive Surgery*, while enrollment for the 56-patient Nirvana trial is pending) & the elegantly-named JelliSee IOL as developed by private VA-based JelliSee Ophthalmics. JelliSee claims that its IOL can achieve > 7 diopters of lens accommodation with only 0.2mm changes in lens diameter (so fairly large changes in focal plane are achievable with small adaptable changes in lens geometry)
  - The OmiiVu IOL as developed by CA-based Atia Vision (private). The IOL performed well at three-year follow-up in a nineteen-patient post-cataract surgery trial that was reported earlier this month at the American society of Cataract & Refractive Surgery annual meeting, with patients sustaining mean binocular uncorrected distance visual acuity of -0.11MAR (short for minimum angle of resolution, which is a measure of how well the eye can distinguish between two points in space without perceiving them as being a single point) & mean best-corrected distance visual acuity of -0.17MAR, both of which reflect favorably on the lens' magnitude of effect & duration of effect.
  - The OmniVu & the AVL200 IOL as developed by CA-based private firm Atia Vision (a three-month 60-patient visual acuity study is ongoing in India, data by H226).

- The Lumina lens developed by Netherlands-based private firm AkkoLens International BV (one-year visual acuity data from a 25-patient Phase III trial in Spain that was completed in Q423 was published for Lumina IOL in Apr/25 in the *Journal of Refractive Surgery)*.
- The Opira A-IOL developed by CA-based private firm & ForSight Labs spin-out ForSight Vision6 (a 200-patient visual acuity trial was apparently ongoing during 2020-to-2024 according to the US NIH's clinical database, but no updates since then are in the public domain; design changes in the lens were planned according to a Apr/24 article in *Ophthalmology Management*).

- **AI-based drug discovery just keeps on rolling – Merck & Google forge a new alliance in this arena.** Two industry giants in their respective disciplines, NJ-based pharma giant Merck (MRK-NY, NR) & CA-based IT giant Google Cloud (part of Alphabet [GOOG-Q, NR]) consummated a new AI-based partnership for which details were extremely vague, probably intentionally so, with the press release from both partners simply stating that a platform based on Google's existing Gemini Enterprise technology will be developed that has applications to R&D, manufacturing, commercial & corporate functions (so everything that Merck does as an organization).
  - We are less interested in the deal itself, since there is nothing for us to analyse other than to acknowledge that cumulative potential deal value of US$1B is again at blockbuster levels as so many of the AI-related deals we have described in these pages have been, but it is nonetheless likely that AI-based drug discovery could focus more intently on oncology drug development, with Merck announcing the creation of a distinct oncology business unit in a corporate update shared last quarter.
  - Undoubtedly, this decision is motivated by the sustainable success achieved for the firm's leading anti-PD1-targeted mAb pembrolizumab/Keytruda (also its subcutaneously-injectable pembrolizumab-hyaluronidase combination Keytruda Qlex) that generated FQ425 sales of US$8.4B last year. In Merck's FQ425 corporate update presentation, it identifies seventeen pipeline assets that are on pace to be FDA-approved/launched in F2027/28, twelve of which are anti-cancer therapies (four are targeting infectious disease & one [the Tie2/VEGF agonist drug MK-8748] is targeting ophthalmic conditions).
  - The Merck-Google Cloud alliance is less interesting to us on its own than it is as an event that re-focuses us on the overall drug discovery continuum & AI's role within its. Accordingly, we were interested in just how successful AI-based drug discovery has been so far, not just in identifying leads which conventional drug screening/synthesis was already able to achieve in abundance, but in identifying molecules that successfully navigated preclinical-Phase I/II & perhaps even Phase III clinical testing.
  - The task of going through every drug developer's clinical/commercial Rx portfolios in search for evidence that some pipeline drugs originated from AI initiatives seems a bit daunting to us, so as a shortcut, we are herein referring to an article published by the Boston Consulting Group in Jun/24 in *Drug Discovery Today*, in which analysis showed that 80-to-90% of AI-derived drugs successfully navigated Phase I clinical testing (so whatever AI platform was deployed, it was able to accurately predict ADME-Tox characteristics, specifically on organ [liver, kidneys, heart] toxicity, that allowed for more extensive clinical testing thereafter).
  - Additionally, at the time of publication of the article, BCG claimed that AI drugs in its database achieved success in Phase II clinical testing of about 40%, implying of course that AI platforms of various types were already able to predict clinical activity for AI-discovered drugs just from assessing relevant molecular structural motifs (or binding sites on already-characterized molecular targets) & referring back in the medical literature to how those motifs/targets performed in published biochemical assays or clinical studies. We presented figures from the *Drug Discovery Today* article before, but as a reference point in the analysis to follow, we show in Exhibit 5 a summary of AI-based activities during F2014-to-F2023 that document considerable momentum in AI-based clinical trials activity, momentum that has undoubtedly accelerated in recent quarters.
  - But moving on from this BCG analysis, we found a separate analysis of AI-based drug discovery that we thought useful to share, as published in May/24 in the journal Science by staff writer Derek Lowe – therein, the author describes twenty different small-molecules or biologics that were in active clinical testing at the time of publication. Herein, we will review that list of AI-discovered drugs & update development status of each in turn. We ourselves find development details of the clinical-stage therapies described below to be interesting for our own purposes – you may not – but the key takeaway

for us is that AI-discovered therapies are achieving substantial success in subsequent stages of clinical testing, providing validating evidence for the power of AI across the entire drug discovery/development continuum. Its relevance, unsurprisingly, is well-positioned to grow exponentially in coming periods:

Exhibit 5. AI-Discovered Drugs/Targets Are Advancing Rapidly Through Formal Clinical Testing



Source: *Drug Discovery Today (June/2024)*

- ATH-063. This orally-active G9A methyltransferase-inhibiting small-molecule was discovered by CA-based Athos Therapeutics (private) using its AthosOmics.AI platform. The drug is targeting inflammatory bowel disease, with a 120-patient Phase II ulcerative colitis trial about to enroll its first patient later this quarter. The target enzyme is part of a group of histone methyltransferases but with its specific activity directed at attaching methyl groups to a lysine side chain at position #9 in the amino acid sequence of histone H3, an activity that has a putative role in regulating gene expression in cancer cells.

- The primary endpoint is expected to be three-month clinical remission rate as assessed by the ulcerative colitis disease severity score, with data on pace to be generated by end-of-F2028. Interestingly, no published data are available for this drug but Athos funded a 76-patient Phase I trial that concluded in Oct/24, showing the ability to increase the number of circulating regulatory T-cells along with up-regulating at least six different genes that are known to influence the anti-inflammatory activity of this T-cell subpopulation.

- BEN-8744. This orally-active phosphodiesterase 10 inhibiting drug is also targeting ulcerative colitis, with Luxembourg-based innovator Benevolent AI (ticker was BAI-AS, NR, but it merged with Osaka Holdings [2502-JP, NR] in Feb/25) reported Phase I data from a 54-patient trial back in Mar/24. The trial exclusively enrolled healthy volunteers so it provided no insights on efficacy in inflammatory gastro-intestinal disorders but PK data showed that twice-daily dosing was appropriate for the formulation being tested & there were no major side effects that argued against any of the doses that were tested in the trial.

- But the drug has not yet advanced into formal Phase II ulcerative colitis testing, though probably less due to any deficiencies in BEN-8744 itself & more influenced by the corporate reorganization undertaken back in Dec/24 that

led to the firm's merger with Osaka as implied above. At this point in our analysis of BenevolentAI & BEN-8744, the narrative gets lost in corporate activities & becomes less focused on BEN-8744 pharmacology itself, so we surmise based on available evidence that the drug remains sufficiently attractive to advance into Phase II testing based on merits of the drug alone. We do not see any published data on BEN-8744 in the medical literature, at least not under that name.

- BDTX-4933 (S241656). This orally-active Braf-inhibiting drug developed by MA-based Black Diamond Therapeutics (BDTX-Q, NR) does have a published clinical history & is in fact now partnered with France-based specialty pharmaceutical firm Servier (private) in a US$780M development alliance announced back in Mar/25 (hence the change in name of the drug to S241656). We already know that the drug crosses the blood-brain barrier (the way this tends to be described in scientific discourse now is that it is CNS-penetrant) & it selectively targets activated forms of the oncogene-derived protein Raf while also inhibiting proliferation of tumor cells harboring mutated forms of the Braf, Kras & Nras oncogenes.

- Loyal readers of our Healthcare Weekly will recall that we emphasized the relevance of Ras mutations to Oncolytics Biotech's (ONCY-Q, Spec Buy, PT US$3.00) pelareorep for which selective inhibition of tumor growth in Ras mutation-harboring cells formed the basis of a famous 1998 paper published in the journal Science that formed the basis for the founding of the firm. And we would be remiss not to re-emphasize the importance of Ras biology to the positive Phase III pancreatic cancer survival data recently generated by Revolution Medicines (RVMD-Q, NR) for its small-molecule drug daraxonrasib in the RASolute 302 trial; that trial specifically puts Ras biology squarely in the focal plane of multiple oncology drug developers, Oncolytics included, that have been mistakenly de-emphasizing the relevance of Ras to cancer drug development.

- But shifting back to BDTX-4933/S241656, seminal Phase II data from a 554-patient solid tumor trial should be available by mid-F2028. Multiple PK endpoints are still being determined in the trial, but of the key endpoints that we conventionally monitor in Phase II oncology studies, objective response rate & survival will be tracked for up to five years so final data from all enrolled subjects (the trial started in FQ223 but only 23 patients were enrolled by Sept/25 according to an abstract published in Jan/26 in *ASCO Gastrointestinal Cancers Symposium* conference proceedings) will probably not be available until F2029/30. But our key conclusion is that this AI-discovered drug is clearly advancing well through a sizable efficacy-based solid tumor study for which early preclinical-Phase I data were sufficiently positive to incentivize Servier's interest in the program, perhaps including an abstract describing preclinical BDTX-4933 data in Oct/22 in the *European Journal of Cancer*.

- BDTX-1535/silevertinib. Another small molecule from Black Diamond Therapeutics' portfolio is in this case an orally-active EGFr-inhibiting drug for which much more published data are available for review. The drug targets multiple mutated forms of EGFr that through being mutated are no longer regulated in the way that wild-type EGFr is & thus is constitutively activated to a degree that leads to unregulated growth/division in tumor cells harboring those mutations. BDTX-1535/silevertinib's foundational pharmacology is described in a few recent papers, including but not limited to a Nov/24 study published by University of Munich researchers in *Translational Cancer Research*.

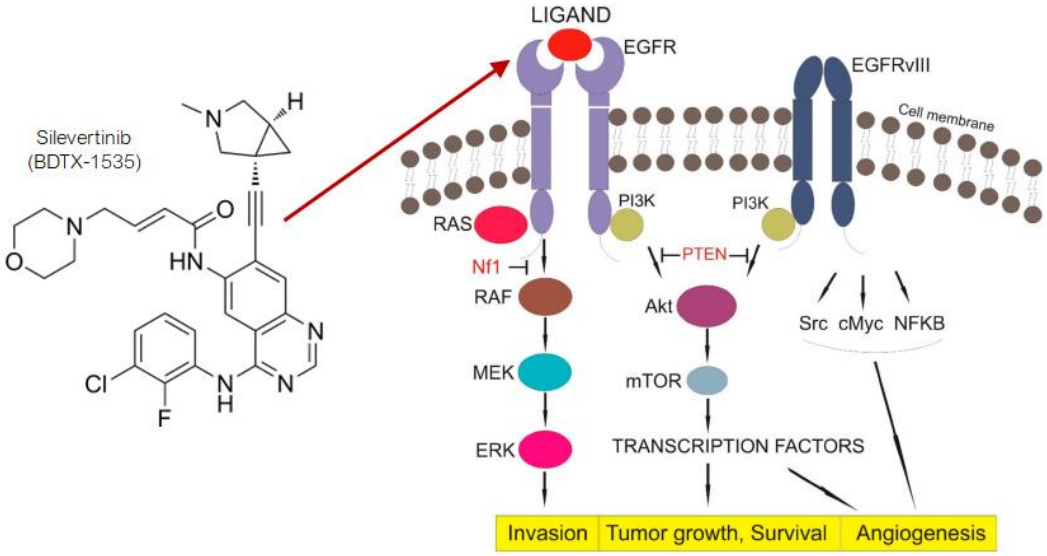
- The drug is currently being tested in combination with temozolomide (Merck/Schering's [MRK-NY, NR] Temodar) in a 162-patient Phase II newly-diagnosed glioblastoma trial, with specific emphasis on patients exhibiting unmethylated forms of the enzyme MGMT (short for O6-methylguanine-DNA methyltransferase; patients with methylated forms of this enzyme are more responsive to Temodar). Twelve-to-eighteen month progression-free survival & overall survival data are expected during F2029.

- A separate 82-patient Phase I/II trial that is testing both newly-diagnosed & recurrent high-grade glioma is also enrolling subjects, all of which are harboring EGFr mutations in the form of either alterations or fusions & not point mutations as are also frequently observed in this cancer form. One-year progression-free survival & overall survival data are expected by end-of-F2027.

- And thirdly, Black Diamond is funding a 200-patient Phase II glioblastoma & non-small-cell lung cancer trial for which final survival data are expected later this year but for which interim data were reported in press-release form back in Dec/25. In that update, Black Diamond reported that overall tumor response rate was 60% (assessed conventionally using CT-imaging-confirmed RESIST 1.1 criteria) & CNS response rate of 86% (which means extent

of brain metastasis, as assessed using so-called response assessment criteria for brain metastasis [RANO-BM]) in forty-three evaluable lung cancer patients. Interestingly BDTX shares declined sharply in response to that Phase II update, though did so within the context of a stock that returned >130% over the T6M period.

Exhibit 6. Molecular Structure For BDTX-1535/Silevertinib & Its Proposed Mechanism Of Action



Source: *MedChemExpress, Society of Neuro-Oncology 2026 conference*

- CEL-383/ABBV-8736. This anti-TREM1 mAb as developed by Celsius Therapeutics (part of AbbVie [ABBV-NY, NR] since Jun/24) is targeting irritable bowel disease (IBD). TREM1 is short for triggering receptor expressed on myeloid cells 1. The drug performed well in an initial 48-patient Phase I healthy volunteer trial & we assume that Phase II IBD either in ulcerative colitis or Crohn's disease is pending. AbbVie now identifies this drug as ABBV-8736 & as a Phase II Crohn's disease asset in its pipeline. The drug showed potent inhibition of TREM1 signaling (which influences multiple pro-inflammatory pathways) in preclinical studies & was discovered using Celsius' proprietary single-cell observations for precision effect (SCOPE) platform.

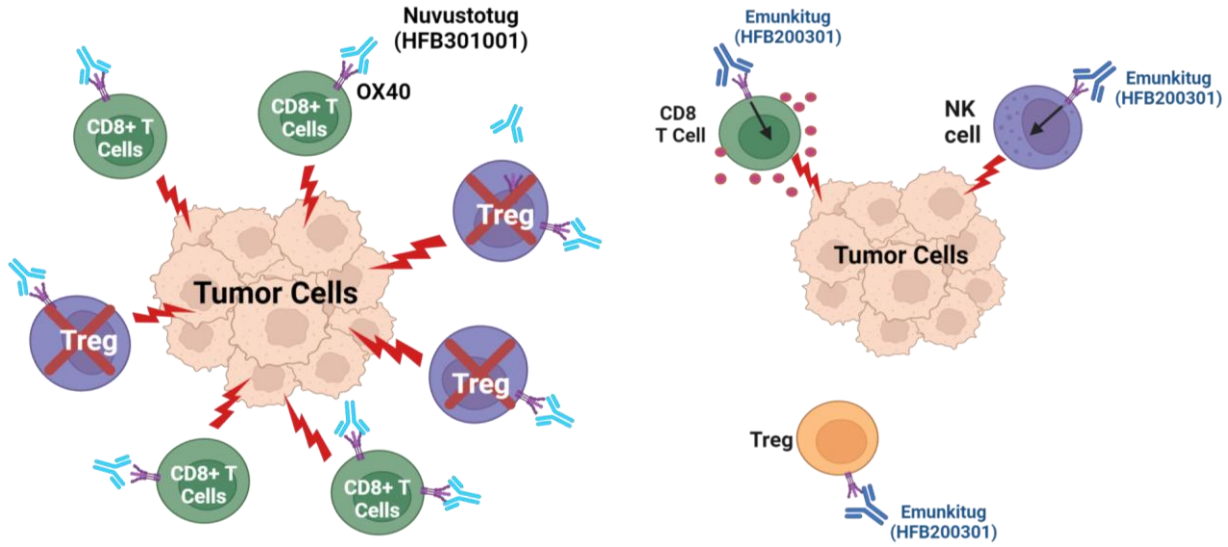
- Bapotulimab/BAY1905254. This anti-ILDR2 mAb as developed by Bayer AG (BAYN-DE, NR) is targeting solid tumors, specifically in a now-completed 60-patient head & neck cancer trial when used in combination with Merck's pembrolizumab/Keytruda. ILDR2 is short for immune checkpoint immunoglobulin-like domain-containing receptor-2, a T-cell receptor protein that by being bound to bapotulimab has its ability to inhibit T-cell activity impeded, thus allowing cytotoxic T-cells to exert anti-tumor activity, or so the theory goes. Uninhibited ILDR2 negatively regulates T-cell responses as part of its normal immunological activity. Bapotulimab/BAY1905254 is characterized in a few papers in the medical literature, including but not limited to a 2020 preclinical study published in *Cancer Immunology Research* by Bayer AG researchers.

- Nuvustotug/HFB301001. This anti-OX40/CD134 mAb as developed by MA-based HiFiBio Therapeutics (private) was actually undergoing testing in a 31-patient Phase I/II advanced solid tumor trial before the trial was terminated back in 2024, for reasons that HiFiBio claims were due more to reprioritization of clinical priorities & not related to nuvustotug's pharmacology as such. The mAb was discovered using HiFiBio's drug intelligence science (DIS) platform in combination with its B-cell screening platform CelliGo & its bioinformatics software branded as AbSolution. OX40 is a sub-category of receptors that are related to tumor necrosis factor (TNF) but which are exclusively expressed on the surface of various T-cell populations; accordingly, OX40 agonists should in theory kickstart T-cell immunity in a way that enhances anti-tumor activity. Despite discontinuation of the aforementioned trial, nuvustotug is still identified as a relevant drug in HiFiBio's R&D pipeline.

- Emunkitug/HFB200301. This anti-TNFR2 mAb (TNFR2 is short for tumor necrosis factor receptor 2) is like OX40 also predominantly expressed on various T-cells, but also natural killer cells & myeloid cells. This mAb is undergoing

testing in combination with the anti-PD1 mAb tislelizumab/Tevimbra (CA-based BeOne Medicines GmbH; ONC-Q, NR) in a 72-patient Phase I/II advanced solid tumor trial for which response rate/survival/biomarker data are expected by end-of-F2026. The mAb & the aforementioned Phase I/II trial were most recently described in Sept/25 in the ESMO journal Annals of Oncology, with interim data showing a tight association between proximity of immune cells expressing PD1 to those expressing TNFR2 & therefore to the probability of clinical benefit. PD1 & TNFR2 expression profiling is thus likely to be a key element in predicting emunkitug/tislelizumab responsiveness in future clinical trials

Exhibit 7. Proposed Mode Of Action For HiFiBio's Nuvustotug & Emunkitug



Source: *HiFiBio Therapeutics*

- HFB200603. This anti-BTLA mAb (short for B- & T-lymphocyte attenuator, expressed unsurprisingly on the surface of B- & T-cells; structurally related to PD-1 & to another immune cell antigen CTLA-4 to which Bristol Myers Squibb's [BMY-NY, NR] ipilimumab/Yervoy is targeted) is also developed by HiFiBio Therapeutics & like emunkitug/HFB2000301 is undergoing testing in advanced solid tumors in combination with PD1-targeted tisleklizumab/Tevimbra. Patient enrollment is completed & three-month tumor response/survival data should be available imminently. This study was also described at an interim stage in Annals of Oncology, but in an earlier issue published in Sept/24, & HFB200603 was itself separately described in an abstract presented at the 2022 AACR meeting. Taking all three of the HiFi mAb portfolio drugs in combination, we will be watching for any advances from the firm's DIS platform, which we assume is not intrinsically limited to the mAbs that it has already identified using this AI-enabled mAb/antigen-selection platform.
- HST-1011. This CBL-B-targeted small-molecule drug as developed by private MA-based drug developer HotSpot Therapeutics is targeting advanced solid tumors in a 77-patient Phase I/II trial for which response rate/survival/biomarker data are expected by end-of-F2026. HST-1011 is also being combined with an anti-PD1 mAb (in this case FDA-approved cemiplimab/Libtayo developed by NY-based Regeneron Pharmaceuticals [REGN-Q, NR]). CBL-B is short for Casitaa B-lineage lymphoma proto-oncogene-b, an immune-modulating receptor that is part of the E3 ubiquitin ligase family that is separately targeted by other cancer drug developers that we have described in prior Healthcare Weeklies. Like so many mAbs we described above could have activity in regulating T-cell & natural killer cell activity within a tumor microenvironment.
- HMBD-001. This anti-HER3 mAb as developed by Singapore-based private firm Hummingbird Bioscience is targeting in a few Phase II clinical studies, including a 398-patient Phase II squamous cell carcinoma trial that will combine HMBD-001 with cetuximab/Erbitux & docetaxel/Taxotere, for which response rate/survival data are expected by end-of-F2027. Two other trials that are fully-enrolled include a 68-patient Phase I/II solid tumor trial

targeting genetically-defined patients harboring fusion mutations in the NRG1 (neuregulin 1) gene or mutations in HER3 itself; two-year response rate data are expected by early F2031.

- As well, an 81-patient Phase I/II solid tumor trial that is sponsored by Cancer Research UK & not by Hummingbird itself is expected to generate four year survival data imminently. The firm has multiple AI-enabled mAbs in its pipeline, including the anti-VISTA (short for V-domain immunoglobulin suppressor of T-cell activation; blockade of this receptor promotes type I interferon signalling) mAb HMBD-002 that was just licensed to Australia-based Percheron Therapeutics (PER-ASX, NR), for which HMBD-002 is now one of its leading pipeline assets. Percheron describes in its Feb/26 investor presentation a 48-patient Phase I solid tumor trial in which it will test both HMBD-002 monotherapy with HMBD-002/pembrolizumab anti-PD1 checkpoint inhibition, with tumor response/survival data possibly available in F2028.

- REC-3964. This *Clostridium difficile* toxin B-targeted diazepinedione analog as developed by UT-based Recursion Pharmaceuticals (RXRX-Q, NR) is of course targeting GI-based *C.difficile* infection & thus is positioning itself to compete with first-line metronidazole (multiple generic manufacturers), second-line vancomycin/Vancocin (ANI Pharmaceuticals [ANIP-Q, NR] or fidaxomicin/Dificid (Merck/Cubist [MRK-NY, NR]) & third-line antibody-based therapies like Merck's bezlotoxumab/Zinplava. The drug was undergoing early first-in-human testing in a small Phase I trial that was terminated last year & with Recursion not identifying this drug in its pipeline update in Feb/26, we assume that other AI-discovered assets are now driving ahead in preference to REC-3964.

- Based on review of Recursion's 2005 10K filing, its pipeline is now led by MED1/2-targeted familial adenomatous polyposis-targeted REC-4881, CDK7-targeted anticancer drug REC-617 & RBM39-targeted anticancer drug REC-1245, all of which emanate from the firm's AI Operating System. Recursion is partnered with Sanofi (SNY-NY, NR; through Recursion's legacy acquisition of UK-based Exscientia [ticker was EXAI-Q, NR] in Aug/24) on a few projects, independent of a separate alliance more focused on CRISPR knockout maps & creation of stem-cell-derived neuronal cell therapies in partnership with Roche/Genentech (ROG-SW, NR). Accordingly, REC-3964 appears to be more of a transient setback than a foundational one & Recursion's AI-based pipeline while still early-stage is deep & seemingly expandable.

- VRG-50635. This phosphoinositide-3-kinase-inhibiting small-molecule drug actually targets a specific isoform called PIKfyve as developed by Verge Genomics (private). Here is an example of an AI-discovered drug that unfortunately did not lead swiftly to positive clinical outcomes, in this case in targeting amyotrophic lateral sclerosis, an indication for which there may be insufficient chemical/medical/clinical data on which to base an AI model. As outlines in a Dec/25 editorial in the journal *Science* (coincidentally authored by Derek Lowe whose work inspired this AI drug discovery overview), the drug failed a 54-patient Phase I ALS trial completed last year & Verge itself is seeking to partner its AI platform, which is apparently more focused more on using algorithms for gene mapping than on other pharmacologic inputs, to other drug developers.

- Other AI-discovered clinical assets that we will be tracking going forward include rentosertib/INS018-055 (a TNIK-inhibiting small-molecule as developed by InSilico Medicine [3696-HK, NR] that just consummated a blockbuster alliance with Eli Lilly last quarter, as described in a recent Healthcare Weekly; the drug is targeting idiopathic pulmonary fibrosis in a 40-patient Phase II trial, as we previously described), omilancor/BT-11 (a small-molecule activator of the LANCL2 protein as developed by NImmune Biopharma [private] that was targeting Crohn's disease but that study was withdrawn in 2022; the drug is still flagged as a Phase II-stage ulcerative colitis asset, pending availability of capital), NX-13 (a small-molecule NLRX1 agonist drug as developed by AbbVie/Landos Biopharma [ABBV-NY, NR] that was targeting ulcerative colitis but an 81-patient Phase II ulcerative colitis trial was discontinued in 2025), NIM-1324 (a small-molecule drug that is also a LANCL2 activator, also developed by NImmune, while targeting rheumatoid arthritis & lupus) & NEU-411 (a small-molecule LRRK2-inhibiting drug as developed by CA-based precision medicine firm Neuron23 [private] that is targeting early Parkinson's disease in the 150-patient NEULARK trial; data in FQ427).

- Nektar's rezpegaldesleukin generates positive Phase II alopecia data, thus revealing to us that long-acting modified interleukin-2 formulations have broad medical utility – read-through to Cipher & Medicenna. CA-based Nektar Therapeutics (NKTR-Q, NR) reported 52-week data from the 16-week blinded extension period for its Phase IIb REZOLVE-AA trial testing the firm's PEGylated interleukin-2 formulation rezpegaldesleukin as a therapy for treating severe-to-very-severe alopecia

areata. This long-acting interleukin-2 is designed in this indication to preferentially expand regulatory T cells. Patients who had shown hair growth at Week 36 but had not yet achieved ≥80% scalp coverage (SALT Score >20) were eligible to continue at their induction dose through Week 52.

- This program is of interest to us for two reasons – first of all, alopecia does overlap if indirectly with dermatology indications that would fit rationally into the commercial portfolio of ON-based dermatology-focused specialty pharmaceutical firm Cipher Pharmaceuticals (CPH-T, Buy, PT C$19.00) that we of course cover. Atopic dermatitis & moderate-to-severe plaque psoriasis are two other dermatology indications for which Nektar may advance rezpegaldesleukin. Indeed, a 396-patient Phase II atopic dermatitis trial (the REZOLVE-AD trial) is already fully-enrolled & poised to generate symptom resolution data by end-of-F2026.

- But also, long-acting interleukin-2 is a concept embedded into ongoing Phase II oncology clinical programs sponsored by ON-based biologics developer Medicenna Therapeutics (MDNA-T, NR), with the firm still advancing its 115-patient Phase II ABILITY-1 solid tumor trial testing its albumin-fused genetically-modified interleukin-2 formulation MDNA11 (Medicenna separately reported positive PK dosing data at the AACR 2026 conference for its anti-PD-1/interleukin-2 bifunctional superkine MDNA113, with the biologic's engineered masking protein domain keeping interleukin-2 in a quiescent state until it is unmasked within a solid tumor micro-environment, an intriguing concept that mitigates the cytokine storm side effects that often accompany interleukin-2 monotherapy).

- Of 31 patients entering the extension phase, 27 were on active drug at two distinct dosage strengths (either 18 µg/kg or 24 µg/kg) and four were on placebo; virtually all enrolled patients (94%) completed one-year follow-up without identifying any treatment-emergent adverse events other than transient redness/erythema at the injection site, which is common for injectable therapies & likely not unique to rezpegaldesleukin. In parallel with its alopecia data update, Nektar consummated an upsized US$325M equity offering this week, mimicking Revolution's equity offering in the wake of its Phase III advanced pancreatic cancer data last week after which it raised US$2B in new equity capital in response to its own positive clinical advance, in that case for Ras-targeted small-molecule daraxonrasib.

- But shifting back to respegaldesleukin/alopecia, the extension phase delivered solid evidence of deepening response in partial responders & the associated capital raise shows us that capital markets agreed with that assessment. From Week 36 to Week 52, new SALT≤20 response (≥80% scalp coverage) was achieved by 29% of 18 µg/kg patients & 31% of 24 µg/kg patients as compared to no response at all in placebo patients. In the overall mITT-adapted population (ITT, or intent-to-treat, means that all enrolled subjects are assessed at final data analysis, with patients who withdraw from a study categorized as failing the therapy under clinical consideration; such patients can be excluded from final data analysis under what is called per-protocol analysis. Both forms of biostatistical analysis are useful & provide distinct but overlapping insights into a drug's medical profile), 52 SALT≤20 response at one-year follow-up rose to 25.8% (18 µg/kg) and 27.6% (24 µg/kg) from 14.8% and 15.6% at Week 36, as compared to stable 6.7% response rate for placebo patients. SALT≤30 response (≥70% scalp coverage) climbed to 30.2% and 35.0% from 21.9% and 29.0%, vs 8.4% of placebo patients. Data were statistically significant in all analyses.

- SALT50 and SALT30 (relative improvement from baseline, so subtracting placebo response rate from treatment response rate) at one-year follow-up were 37.7%/38.8% and 45.6%/47.6% for the two active arms, vs 13.6% and 24.2% for placebo. The trajectory is consistent with the deepening pattern Nektar has previously reported in its REZOLVE-AD atopic dermatitis study (see above), where EASI-100 rates more than doubled between Week 16 and Week 52 on monthly and quarterly maintenance.

- If you asked us a few years ago just how relevant modified long-acting interleukin-2 formulations could be in non-cancer indications, alopecia would not have been on our Bingo card & yet data described above is clearly favorable to Nektar's interleukin-2 variant in at least one non-cancer medical market. Mechanistic rationale for interleukin-2, modified or not, centers on its ability to restore hair follicle immune privilege, which collapses in alopecia through infiltration into hair follicles of cytotoxic T cells, with an accompanying depression of infiltration of regulatory T-cells to mitigate cell-mediated activity in that region (we surveyed two papers for insights on this concept, one published by Bertolini's team in 2020 in *Experimental Dermatology* & another by Shin's team in 2013 in the *Journal of Dermatological Science*).

- Accordingly, rezpegaldesleukin's regulatory T-cell-mediated activity is clearly differentiated from the other therapies that target the indication through inhibition of the JAK pathway, with alternative orally-active JAK inhibitors including

baricitinib/Olumiant, ritlecitinib/Litfulo & deuruxolitinib/Leqselvi. Based on product monograph data we reviewed, each of these therapies delivers 35-40%, 23%, and 'numerically higher SALT≤20' response rates at comparable duration of follow-up, respectively. However, each has non-trivial side effects that include cardiovascular risk, thrombosis, infection & even cancer emergence, with high relapse rates once therapy is discontinued. A mechanistically defined biologic like rezpegaldesleukin could deliver comparable hair regrowth without JAK-class side effect profile & thus emerge as a first-line (meaning before JAK inhibitors are indicated) therapy in severe-to-very-severe disease. One of these alternative biologics interestingly is Sanofi/Regeneron's (SNY-NY, NR) dupilumab/Dupixent, on which we have commented many times in regard to EP104GI's competitive landscape in eosinophilic esophagitis, clearly not a dermatologic indication but one with pathophysiological overlap through being mitigated via immunological intervention.

- **Minimal read-through to Eupraxia Pharmaceuticals (EPRX-Q, Buy, PT US$12.75).** Management flagged food allergy and other TH2-mediated diseases as potential adjacent markets for the Treg platform, but EoE was not identified as a near-term development priority and would sit behind moderate-to-severe AD (Phase III ZENITH-AD initiating Q2/26), AA (Phase III planned 2026), asthma, and T1D in the development queue. More importantly, the Treg-expansion thesis has already been tested and underperformed in EoE via Revolo Biotherapeutics' (private) peptide IRL201104, which expanded both regulatory B and T cells in its 36-patient Phase IIa but failed to translate the histologic signal into Dysphagia Symptom Questionnaire separation from placebo (8 mg arm median DSQ -6.94 vs -3.91 placebo; identical 8.3% histologic remission at <15 eos/HPF in the 8 mg and placebo arms). That precedent, detailed in our initiating coverage report on EPRX from Oct/25, sits within our broader observation that single-pathway biologics addressing upstream immune tone (cendakimab, benralizumab/Fasenra, lirentelimab/AK002 or Tezepelumab/Tezspire) have repeatedly delivered histologic response without commensurate symptomatic benefit in EoE, reinforcing our view that EP-104GI's local, sustained-release corticosteroid delivery targets the fibrotic/structural arm of EoE pathology these systemic mechanisms have not addressed. We are maintaining our PT/rating on EPRX.

- **Eli Lilly bids to acquire Kelonia Therapeutics, expanding its suite of cancer-targeted CAR-T therapies in the process.** IN-based pharma giant Eli Lilly (LLY-NY, NR) agreed to acquire Kelonia Therapeutics, a clinical-stage biotech developing in vivo CAR-T cell therapies, for US$3.25B upfront and up to an additional US$3.75B in clinical, regulatory, and commercial milestones. The deal centers on Kelonia's lead program KLN-1010, a potentially first-in-class lentiviral *in vivo* anti- B-cell maturation antigen (BCMA) CAR-T therapy currently in Phase I for relapsed/refractory multiple myeloma. The transaction is expected to close in H2 2026.

  - As we have noted in prior Healthcare Weeklies, our current coverage universe does not at present have any CAR-T therapies in formal clinical testing, but multiple myeloma is an indication that is relevant to a molecular diagnostics firm that we follow closely (MB-based TELO Genomics [TELO-V, NR]) based on our positive view on how useful visualizing telomere architecture can be in diagnosing disease or disease responsiveness to therapy. In last week's weekly, we discussed Allogene's allogeneic (donor-derived, off-the-shelf) CAR-T program in lymphoma, which bypasses the logistical burden of autologous manufacturing by using pre-made donor cells. Kelonia represents a further conceptual step: rather than manufacturing CAR-T cells outside the body at all, KLN-1010 is functionally a one-time intravenous gene therapy.

  - The drug uses an engineered lentiviral vector particle that selectively enters circulating T cells in vivo and integrates a CAR transgene directing those cells against BCMA, a surface protein expressed on myeloma cells. The patient's own immune system then generates CAR-T cells internally, eliminating the need for apheresis, ex vivo cell manufacturing, and the lymphodepleting chemotherapy that preconditions patients for conventional CAR-T infusion. Lentiviral vectors are already the backbone of five of seven FDA-approved autologous CAR-T products; Kelonia's contribution is engineering that integration biology into a direct-infusion, off-the-shelf format.

  - Preclinical work across the broader lentiviral in vivo CAR-T field has demonstrated functional CAR-T generation and B-cell depletion in non-human primates without lymphodepletion (Nicolai & coworkers as published in 2024 in *Blood*). A parallel non-viral approach using lipid nanoparticles to deliver CAR-encoding mRNA has also shown preclinical activity (Hunter & coworkers as published last year in the journal *Science*), though those constructs produce transient rather than stably integrated CAR expression and may require repeat dosing, a fundamentally different therapeutic profile. Lipid nanoparticle delivery systems may sound familiar, as they are also being explored beyond gene therapy contexts. Rakovina Therapeutics (RKV-V, NR), which we have discussed in prior weeklies, is collaborating with NanoPalm (Riyadh,

Saudi Arabia) on AI-designed patterned LNPs for small molecule oncology drug delivery, a related but mechanistically distinct application of the same underlying delivery platform. We assume that a Rakovina-NanoPalm formal relationship is still plausible & pending.

- KLN-1010 was evaluated in the inMMyCAR Phase I dose-escalation trial (NCT07075185) in patients with R/R multiple myeloma who had received at least three prior lines including a proteasome inhibitor, immunomodulatory agent, and anti-CD38 antibody. First-in-human data from the first four patients, presented as a late-breaking plenary abstract at ASH 2025, showed a 100% MRD-negative response rate, with responses sustained through three months in the two patients with the longest follow-up. Responses deepened over time by IMWG criteria, with one patient achieving complete response at a sensitivity level of 10^{-6} at month 5. CAR-T expansion was robust, reaching up to 85% of circulating T cells, despite no lymphodepleting chemotherapy. Safety was notable for an absence of grade 3+ CRS and no ICANS. Persistent memory-phenotype CAR-T cells were observed in bone marrow and peripheral blood, features the investigators noted have historically been associated with durable remissions from ex vivo CAR-T in myeloma (Ho et al., *Blood*, 2025). The FDA cleared an IND for KLN-1010 in January 2026, enabling US site expansion.

- The data remains extremely preliminary: four patients, maximum five months of follow-up, still in dose escalation. Durability is the central open question. The approved autologous BCMA-directed CAR-Ts, ide-cel and cilta-cel, have demonstrated high initial MRD-negative rates, but a majority of patients eventually relapse; five-year follow-up from CARTITUDE-1 showed roughly a third of cilta-cel patients progression-free (Jagannath et al., *Journal of Clinical Oncology*, 2025), with the critical variable being depth and persistence of CAR-T engraftment. Whether in vivo-generated cells, which do not benefit from controlled ex vivo expansion and selection, can sustain comparable engraftment durability remains to be demonstrated at scale.

- At US$3.25B upfront for a four-patient Phase I dataset, this is among the largest bids placed on early-clinical-stage heme-onc assets. The price speaks less to the maturity of KLN-1010's evidence package than to perceived platform value: if the iGPS lentiviral delivery system proves out, it could be retargeted beyond myeloma to other antigens across heme-onc and potentially solid tumors, collapsing CAR-T manufacturing into a single off-the-shelf infusion. The deal also extends a concentrated period of big pharma consolidation in the in vivo CAR-T space specifically.

- Between mid- and late 2025, over US$6.6B in strategic acquisitions closed in the field, including AstraZeneca/EsoBiotec (US$1.0B, lentiviral), AbbVie/Capstan (US$2.1B, LNP/mRNA), Gilead-Kite/Interius (US$350M, lentiviral), and BMS/Orbital (US$1.5B, RNA-based). Among direct competitors, Umoja Biopharma has three programs in clinical trials but has not yet disclosed results, and Interius (now Kite/Gilead) is in Phase I with INT2104 (anti-CD20) in Australia and Europe. Kelonia's ASH plenary data gave it a meaningful first-mover advantage among lentiviral in vivo platforms, and the Lilly bid values that lead accordingly. We will of course be tracking CAR-T innovations both for their increasingly relevant utility & perhaps not just in hematological cancer forms, as well as for their impact on competitive landscape as ascribed to clinical-stage drug developers in our coverage universe.

- More broadly, big pharma validation of the hematology/oncology medical market continues to expand at a geometric pace. he Merck/Terns transaction (US$6.7B, announced in Mar/26) for an oral BCR::ABL1 inhibitor in chronic myeloid leukemia (CML) and Amgen's acquisition of Dark Blue Therapeutics (US$840M, announced in Jan/26) for MLLT1/3-targeting degraders in acute myeloid leukemia (AML) underscore that large pharma views hematologic malignancies as a strategically under-penetrated area worth premium multiples even for early-stage innovation. In coverage-universe context, Medexus Pharmaceuticals (MDP-T, Buy, PT C$8.00) continues to expand GRAFAPEX (Treosulfan) as an HSCT conditioning agent across US transplant centers. GRAFAPEX and KLN-1010 address biologically distinct corners of hematology/oncology: Treosulfan is a myeloablative conditioning agent used in allogeneic transplant for myeloid malignancies (AML/MDS), while KLN-1010 targets BCMA-expressing plasma cells in multiple myeloma, a lymphoid lineage disease. The connection is not mechanistic but thematic: sustained large-cap appetite for hematology assets at all stages of development reinforces the demand backdrop for commercial franchises operating in the space.

- **Roche [ROG-SW, NR] subsidiary Foundation Medicine entered a definitive merger agreement to acquire Saga Diagnostics (private) for up to US$595M.** The deal brings Saga's Pathlight tumor-informed MRD platform into Foundation's existing portfolio, which includes the FoundationOne Monitor ctDNA test. The transaction is expected to close next quarter. Foundation plans to combine Pathlight with Roche's Axelios sequencing and Digital LightCycler PCR platforms to develop a minimal residual disease (MRD) testing solution that can be run at hospital and reference labs globally, rather than requiring

samples to be shipped to a centralized U.S. laboratory as is currently standard for Pathlight and competing platforms such as Natera's [NTRA-Q, NR] Signatera. Our interest in the Roche-Saga transaction, independent of our intrinsic interest, reflects again on TELO Genomics (& tangentially to Perimeter Medical Imaging [PINK-V, Spec Buy, PT C$3.00], as we describe below), as we describe above for the Lilly-Kelonia transaction even though that transaction was more therapeutics-based & not diagnostics-based.

- Recurrence remains a core clinical problem in breast cancer, with local recurrence rates of 3-5% at five years even after lumpectomy with adjuvant radiation (Boughey & coworkers as published in 2022 at the San Antonio Breast Cancer Symposium), rising to approximately 25% in node-positive disease over longer follow-up horizons. Pathlight's core technical differentiator in blood-based identification of tumor DNA is its use of somatic structural variants rather than single-nucleotide variants as ctDNA biomarkers. Structural variants, which include large-scale genomic rearrangements, produce patient- and tumor-specific breakpoint junctions that occur throughout the genome and are linked to genomic instability and tumorigenesis (Elliott & coworkers, published in 2025 in *Clinical Cancer Research*).

- Pathlight combines whole-genome sequencing of a patient's tumor specimen with digital PCR to design personalized assays tracking up to 16 of these structural variants, achieving a limit of detection as low as 0.001% variant allele frequency. This approach bypasses a key limitation of assays looking for single-nucleotide variants, where increasing the number of tracked variants can improve sensitivity but may introduce false positives from non-tumor DNA. For example, a common source is clonal hematopoiesis, in which age-related mutations accumulate in blood-forming stem cells and shed DNA fragments into circulation that mimic tumor signal. Because structural variant breakpoint junctions are unique to the individual tumor and do not arise from these non-tumor processes, false positives are purportedly reduced.

- The foundational clinical dataset is the TRACER study (Elliott & coworkers, published in 2025 in *Clinical Cancer Research*), a retrospective analysis of 100 patients with stage I-III early breast cancer receiving neoadjuvant systemic therapy. ctDNA was detected at baseline in 96% of participants at a median variant allele frequency of 0.15%, and ctDNA detection at cycle 2 of neoadjuvant therapy was associated with higher likelihood of distant recurrence (log-rank P = 0.047). In the postoperative surveillance period, ctDNA was detected prior to distant recurrence in all cases (100% sensitivity) with a median lead time of 417 days. Saga is also running the CATER trial, a Phase II study evaluating whether secondary adjuvant capecitabine can eradicate detectable ctDNA in ER+/HER2- breast cancer patients with persistent MRD after standard curative-intent therapy.

- Within our coverage universe, Perimeter Medical Imaging operates upstream in the breast cancer care pathway, fundamentally reducing the rate of post-op recurrence as opposed to catching it when it does happen. Perimeter's AI-enabled B-Series OCT platform (branded CLAIRE, FDA-approved Mar/26) performs real-time intraoperative margin assessment of excised breast tumors during lumpectomy, reducing the rate of tissue requiring follow-up shaving from 19.9% under standard-of-care visual inspection to 3.8% (Perimeter 206-patient pivotal trial). Saga's Pathlight enters the picture weeks to months after surgery, monitoring for molecular evidence of residual or recurrent disease via blood draw. These are non-overlapping, sequentially complementary technologies: B-Series aims to ensure complete tumor excision at the time of initial surgery, while Pathlight aims to detect microscopic residual disease that evades both surgical and adjuvant interventions. The Saga deal does underscore sustained appetite among large-cap diagnostics acquirers for precision breast cancer tools to reduce recurrence, which is constructive backdrop for Perimeter's ongoing commercial ramp of B-Series into U.S. surgical oncology centers.

- **Biogen acquires Greater China felzartamab rights from TJ Biopharma, consolidating global ownership.** MA-based diversified specialty pharmaceutical firm Biogen (BIIB-Q, NR) agreed to acquire TJ Biopharma's (Private, China) exclusive felzartamab rights in the Greater China region, completing global consolidation of the asset roughly two years after the US$1.15B upfront HI-Bio acquisition that brought felzartamab into Biogen's portfolio. TJ Bio receives US$100M upfront and is eligible for up to US$750M in commercial and sales milestones (total potential consideration up to US$850M), plus mid-single-digit to low-double-digit royalties on net sales in the region.

  - Felzartamab is a fully human IgG1 anti-CD38 monoclonal antibody that depletes CD38-high plasmablasts and plasma cells via antibody-dependent cellular cytotoxicity and phagocytosis (Mayer & coworkers, published in 2025 in *Expert Opinion on Investigational Drugs*). Worth flagging that while CD38 targeting is well-established in heme-onc (daratumumab in myeloma), the Biogen/HI-Bio thesis applies the same biology to B-cell and plasma cell-mediated

autoimmune disease, where pathogenic antibody-secreting cells are the therapeutic target rather than malignant clones.

- The rationale in IgA nephropathy (IgAN) specifically is that long-lived plasma cells are the likely source of pathogenic galactose-deficient IgA1 (Gd-IgA1) and the autoantibodies against it that drive immune complex formation and glomerular injury. IgAN is the most common primary glomerulonephritis worldwide, caused by deposition of IgA-containing immune complexes in the kidney's mesangium, leading to progressive renal damage and, in a significant subset, end-stage kidney disease. This differentiates the CD38 approach from anti-CD20 strategies (e.g., rituximab), which target earlier B-cell myeloid lineages and failed to show benefit in IgAN (Lafayette et al., *J Am Soc Nephrol*, 2017).

- The Phase IIa IGNAZ study (NCT05065970) randomized 54 patients with biopsy-confirmed IgAN who had persistent proteinuria despite already receiving the standard background therapy of renin-angiotensin system inhibitors (ACE inhibitors, which reduce intraglomerular pressure and are the first-line approach to slowing IgAN progression). Patients were assigned across placebo and three felzartamab dosing arms.

- The primary endpoint was change in proteinuria (UPCR) at nine months. Final 24-month data showed sustained proteinuria reduction and reduced eGFR decline versus placebo, with the 9-dose arm demonstrating the most durable responses. Notably, proteinuria reduction persisted up to 1.5 years off treatment, with IgA remaining suppressed even as IgG and IgM recovered to baseline, suggesting selective depletion of the pathogenic plasma cell compartment. The Phase III PREVAIL trial (104 weeks, 454 patients) is currently enrolling, with a primary endpoint of percent change in 24-hour UPCR at week 36. Felzartamab has received Breakthrough Therapy and Orphan Drug designations from the FDA in PMN, and Orphan Drug designation in AMR. The first Phase III readout is expected in H1 2027.

- **Grace Therapeutics receives a Complete Response Letter for GTx-104 despite what we considered to be positive Phase III subarachnoid hemorrhage clinical data.** Earlier this week, the US FDA issued a Complete Response Letter (CRL) to CA-based small-molecule drug developer Grace Therapeutics (GRCE-Q, NR) for its IV nimodipine formulation GTx-104, for which Grace was seeking approval (& presumably still is) for using the drug to treat aneurysmal subarachnoid hemorrhage. Nimodipine itself is a well-known L-type voltage-gated calcium channel blocker, originally developed in the 1980s as an anti-hypertensive agent & currently branded as the orally-active capsule Nimotop by Bayer Healthcare (BAYN-DE, NR). Its chemical analogs nifedipine & nicardipine were genericized long ago but are still occasionally prescribed for treating hypertension. It was clear from the manner in which the FDA feedback was provided (that is to say, not as a Non-approval Letter) that the agency did not have major issues with IV nimodipine's clinical efficacy for the indication but rather had observations pertaining to the drug's quality control & manufacturing/formulation processes (otherwise known as Chemistry-Manufacturing-Controls [CMC]).

  - GTx-104 was filed under the 505(b)(2) pathway, referencing the established efficacy of oral nimodipine (described in multiple peer-reviewed studies including but not limited to Pickard's 1989 paper in the *British Medical Journal*), with IV nimodipine delivery clearly serving as a novel formulation in service of the more rapid onset-of-action desired for treating aneurysmal subarachnoid hemorrhage, an acute rupturing of a brain aneurysm for which fatality rate is high if bleeding is not rapidly attenuated. Grace's pivotal 102-patient Phase III STRIVE-ON trial met its primary endpoint, showing a 19% reduction in drug-related hypotension versus oral nimodipine (28% vs. 35%) with clear superiority on dosing compliance (54% of IV patients achieved ≥95% relative dose intensity vs. 8% of patients receiving orally-active drug).

  - The rejection pattern is notable - when a regulatory thesis rests on reformulation rather than novel pharmacology, CMC and non-clinical characterization become the *de facto* components of an NDA filing on which agency will focus & in our experience, the FDA holds the bar high on CMC metrics for drug formulations to which foundational pharmacology is not in question. Specific CMC deficiencies were not published but for our own interests, we will watch for specific CMC elements that led to Grace's CRL for their implications on our own coverage universe. At present, we are valuing any clinical-stage therapies for which we expect a 505(b)(2) filing to relevant to regulatory risk. It is notable that the medical literature is well-populated with clinical studies espousing the virtues of oral nimodipine for treating aneurysmal subarachnoid aneurysm, going as far back as a 1983 clinical study published in the *New England Journal of Medicine*.

  - As a point of interest (if only to us!), Grace Therapeutics is the re-imagination of QC-based omega-3 formulation developer Acasti Pharma, which we covered in prior years ostensibly for its Phase III-stage phospholipid ester-based krill oil-derived that it code-named CaPre. There was never an omega-3 fatty acid formulation that did not engender

reduction in serum triglycerides with chronic dosing & that should not have been a risk factor in Acasti's two Phase III triglyceride-lowering clinical trials (TRILOGY 1 & 2) & yet it was in both trials. We have allowed this drug & this Phase III program to our rear view mirror for some time now, but Grace's GTx-104 regulatory setback does give us an opportunity to reflect on how many risk factors independent of clinical efficacy there are on the path to a drug approval, even before commercial adoption becomes its own risk factor down the road.

- For CaPre, we speculated at the time that control patients may have been co-administered other triglyceride-lowering agents (perhaps fenofibrate/Tricor or even other FDA-approved omega-3 formulations like Lovaza or Vascepa that were already available at the time), which would be a failure in clinical trial design & vigilance (not relevant to the GTx-104 filing) but another factor could have been that CaPre's omega-3 components (which have carbon-carbon double bonds that are vulnerable to oxidation if not properly stored) may have degraded over time & yet used without regard to that possibility in the trial. If so, that would clearly have been a failure in quality control. The transformation from Acasti to Grace occurred in Oct/24.

Capital Markets Summary

Exhibit 8. EBITDA Or EPS-Positive Canadian Healthcare Stocks

Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 23-Apr	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 [2,4]														
DRI Healthcare Trust	CAD	DHT.UN	55.0	$16.92	931	931	1,523	1,523	7.3x	6.9x	6.6x	NA	7.5x	7.1x
Jamieson Wellness	CAD	JWEL	41.5	$34.14	1,416	1,416	1,867	1,867	11.8x	10.5x	9.4x	22.9x	16.1x	13.8x
K-Bro Linen	CAD	KBL	13.0	$37.71	490	490	796	796	7.7x	7.3x	6.9x	25.4x	18.4x	15.1x
Medical Facilities [1]	CAD	DR	17.6	$12.27	215	294	406	554	6.5x	7.0x	7.0x	21.6x	6.0x	18.3x
Microbix Biosystems	CAD	MBX	138.0	$0.25	35	35	32	32	NA	NA	10.9x	NA	NA	NA
Savaria	CAD	SIS	71.9	$30.11	2,164	2,164	2,366	2,366	13.0x	11.6x	10.6x	31.3x	21.7x	19.2x
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales [2]														
Aurinia Pharma	USD	AUPH	129.9	$16.42	2,134	2,917	1,771	2,422	10.2x	8.1x	6.7x	7.6x	20.7x	15.7x
Bausch Health	USD	BHC	373.5	$5.54	2,069	2,829	30,882	42,219	6.6x	5.9x	6.0x	13.1x	1.3x	1.3x
BioSyent	CAD	RX	11.6	$15.00	174	174	147	147	12.0x	9.5x	8.1x	18.7x	16.0x	13.4x
Cipher Pharma [1]	CAD	CPH	25.3	$13.35	337	461	457	625	18.9x	16.1x	12.8x	12.5x	17.9x	14.1x
HLS Therapeutics [1]	CAD	HLS	31.3	$3.40	106	145	198	271	12.1x	9.8x	8.2x	NA	NA	NA
Knight Therapeutics	CAD	GUD	98.3	$7.43	730	730	697	697	10.3x	9.2x	8.6x	NA	45.7x	29.3x
Medexus Pharma [1]	CAD	MDP	32.0	$2.84	91	124	142	194	10.4x	8.9x	6.4x	NA	NA	8.9x
Profitable Canadian healthcare firms - eldercare services or infrastructure developers														
CareRx	CAD	CRRX	62.9	$3.75	236	236	297	297	9.8x	8.0x	7.1x	9.0x	22.5x	12.3x
Chartwell Retirement	CAD	CSH.UN	324.0	$20.56	6,661	6,661	9,507	9,507	23.7x	18.9x	17.2x	NA	NA	54.1x
Extendicare	CAD	EXE	94.8	$28.34	2,687	2,687	2,705	2,705	15.4x	11.5x	10.1x	25.1x	23.3x	19.9x
Vital Infrastructure	CAD	VITL.UN	250.0	$5.56	1,390	1,390	2,676	2,676	10.3x	12.5x	12.7x	NA	NA	NA
Nova Leap Health	CAD	NLH	87.3	$0.34	30	30	32	32	11.9x	NA	NA	NA	NA	NA
Sienna Senior Living	CAD	SIA	106.0	$22.55	2,391	2,391	3,707	3,707	24.7x	18.5x	16.8x	46.1x	37.6x	32.7x
Profitable Canadian healthcare firms - medical equipment distribution/sales [3]														
Covalon Technologies	CAD	COV	27.6	$1.90	52	52	37	37	25.5x	10.6x	6.8x	53.3x	27.1x	13.6x
Viemed Healthcare	USD	VMD	38.6	$9.51	367	367	504	689	7.4x	5.5x	4.8x	24.7x	19.8x	15.3x
Profitable Canadian healthcare firms - healthcare IT or digital IT services firms														
Healwell AI	CAD	AIDX	295.6	$0.90	266	266	333	333	NA	40.2x	20.4x	NA	NA	NA
Hydreight	CAD	NURS	53.4	$4.20	224	224	214	214	NA	9.4x	7.7x	NA	14.0x	8.6x
Kneat.com	CAD	KSI	96.1	$4.28	411	563	394	394	NA	22.7x	15.4x	NA	NA	NA
Vitalhub	CAD	VHI	63.3	$8.07	510	698	379	379	16.6x	11.1x	9.5x	NA	32.0x	25.6x
Well Health	CAD	WELL	255.5	$4.27	1,091	1,091	1,813	1,813	9.0x	10.2x	9.2x	NA	15.5x	11.3x
Average									**12.8x**	**12.1x**	**9.8x**	**23.9x**	**20.2x**	**17.5x**
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***
Dentalcorp Holdings	***CAD***	***DNTL***	***192.0***	***$11.00***	***2,112***	***2,112***	***3,112***	***3,112***	***10.9x***	***NA***	***NA***	***NA***	***NA***	***NA***
Quipt Home Medical	***USD***	***QIPT***	***44.5***	***$3.65***	***162***	***223***	***235***	***323***	***5.4x***	***NA***	***NA***	***2.1x***	***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

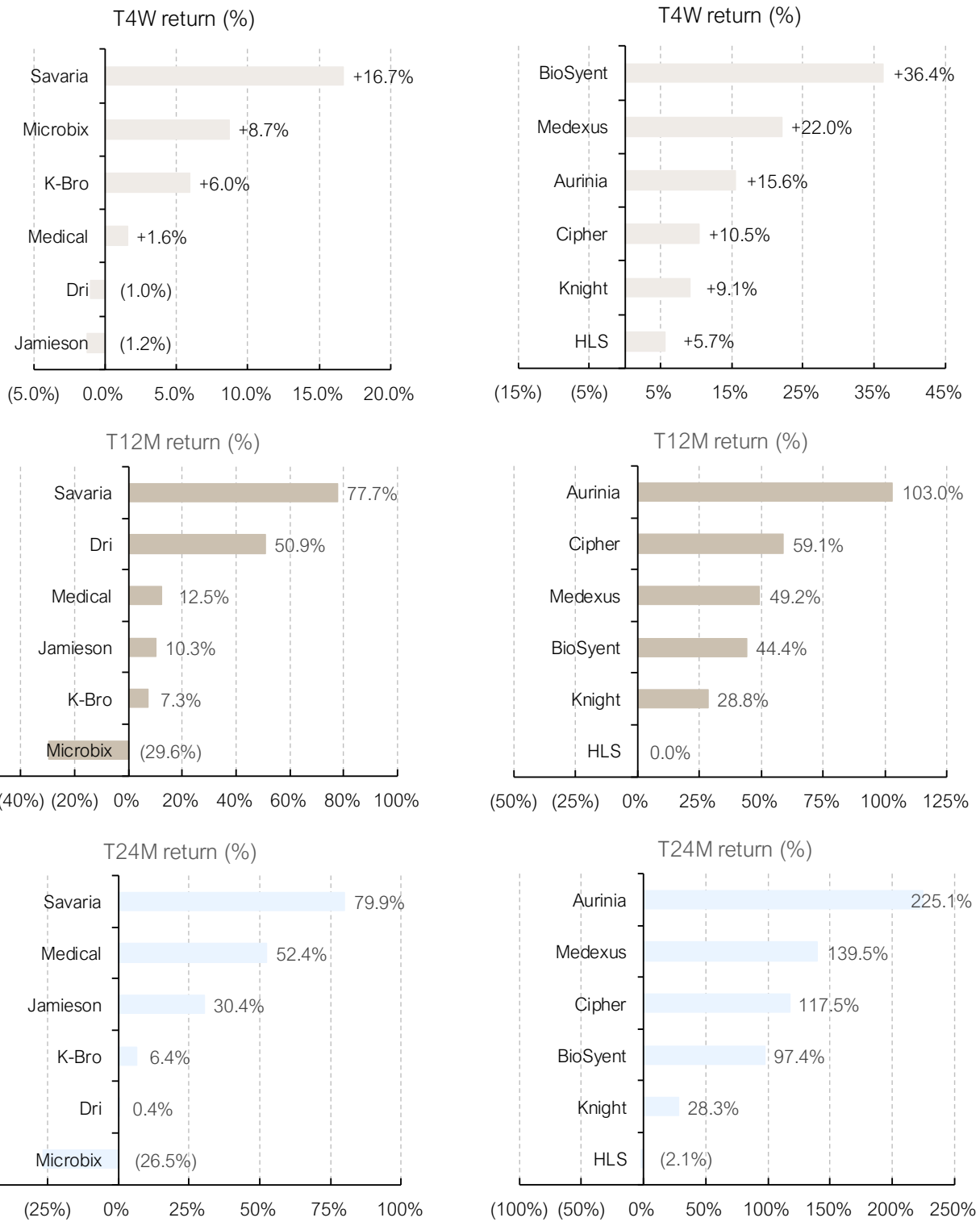
[2] Legacy specialty pharmaceutical firm & coverage stock Theratechnologies (TH-T, THTX-Q) was acquired in Sept/25 by CB Biotechnology/Future Pak for cumulative consideration of US$4.20/shr; Andlauer's acquisition by UPS (UPS-NY, NR) is closed as of Nov/25

[3] Quipt Home Medical was bid to be acquired by Kingswood Capital & Forager Capital for US$3.65/shr in Dec/25, transaction closed in Mar/26

[4] Dentalcorp Holdings was acquired by US private equity firm GRCR LLC in Sept/25 for an EV of C$3.3B (market value C$2.1B); transaction closed in Jan/26

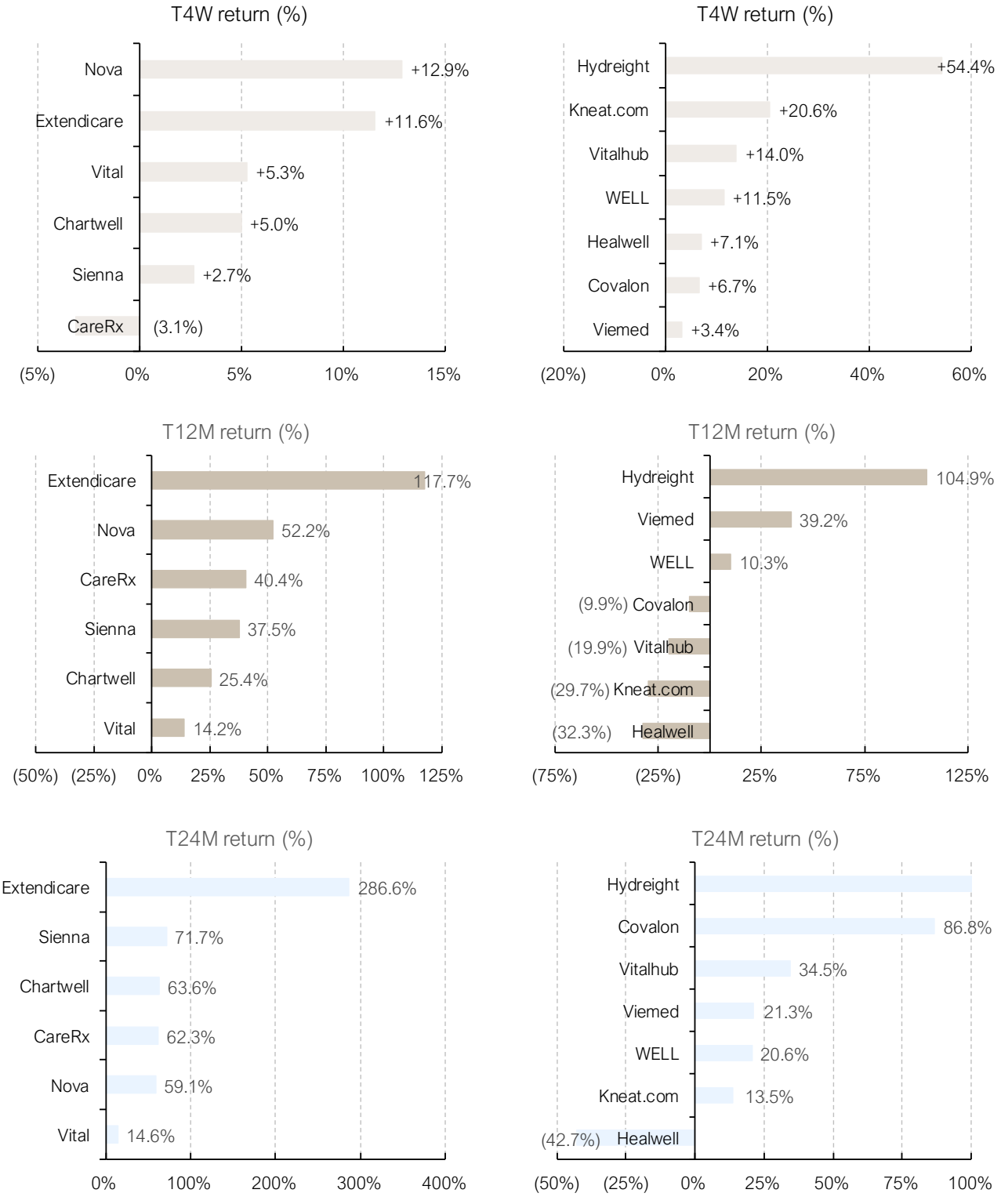
Source: Refinitiv, company reports, Leede Financial

Exhibit 9. 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 10. 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 *(Hydreight [NURS-V, NR] T24M return 1,580%)*

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RECOMMENDATION	NO. OF COMPANIES	%
Buy	9	60%
Speculative Buy	4	26%
Hold	1	7%
Sell	-	-
Tender	-	-
Under Review	1	7%

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
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
Satellos Biosciences | MSCL-TSX	2