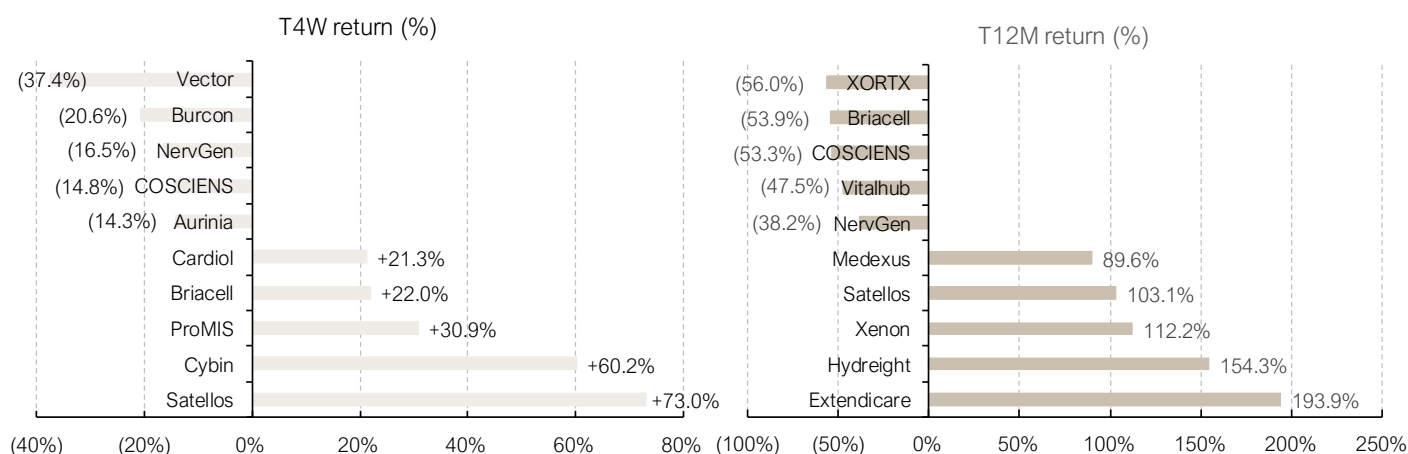


Core Highlights of the Week

Top Movers

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



Source: Leede Financial, Refinitiv

Significant Developments With Relevance To Our Coverage Universe

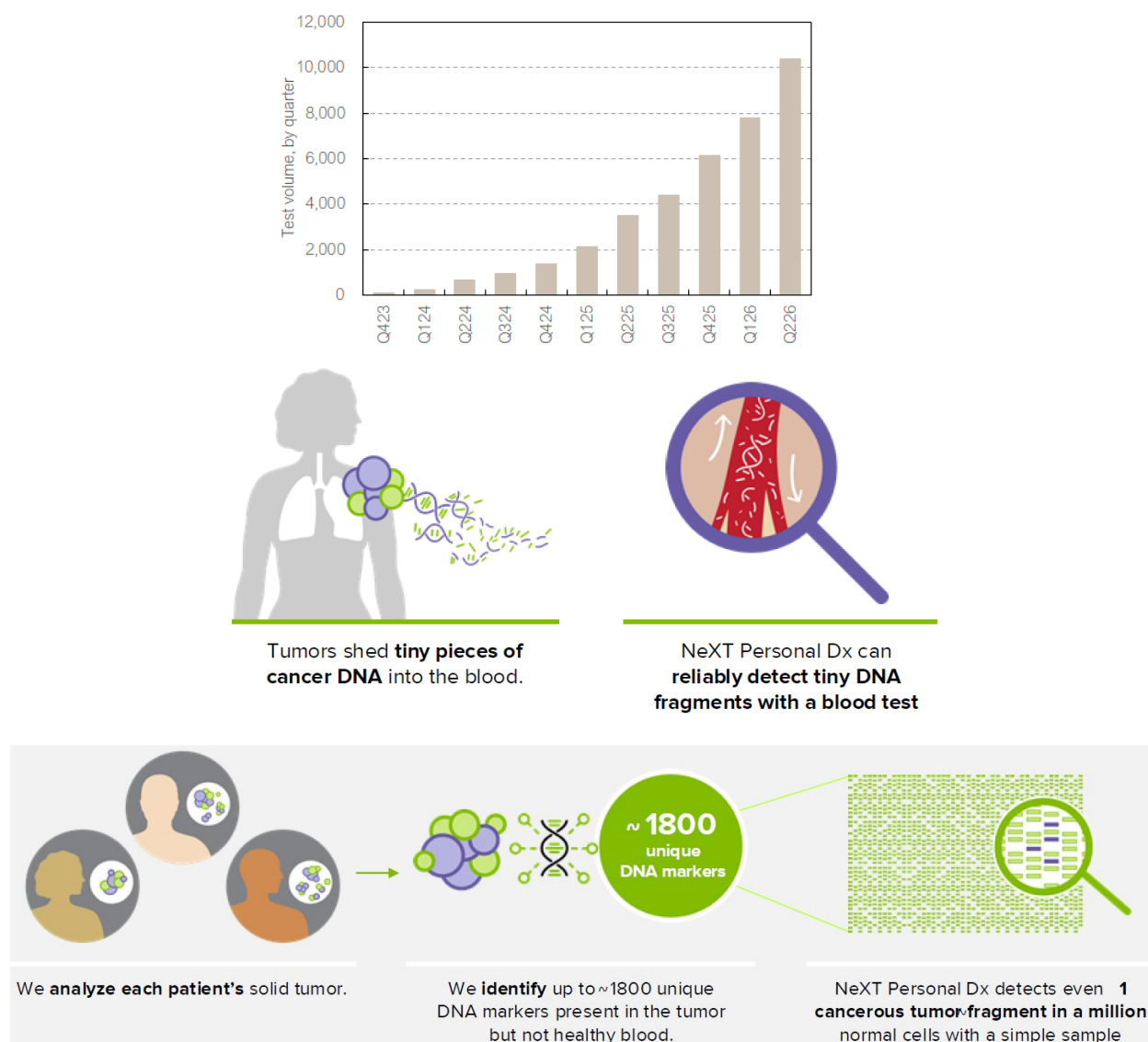
- Cancer diagnostic firms continue to attract interest both from acquirers & from end-market laboratories, with read-through to Telo Genomics.** IL-based AI technology developer Tempus AI (TEM-Q, NR) is acquiring cancer diagnostic developer Personalis (PSNL-Q, NR) in a deal valuing the cancer-focused test developer at an enterprise value of US\$1.5B. Personalis' lead test is focused in identifying cancer patients who following chemotherapy (if for multiple myeloma for example, such therapy would likely be some combination of immunologically-active agents like lenalidomide/Revlimid or pomalidomide/Pomalyst [both sold by Bristol-Myers Squibb/ Celgene; BMY-NY, NR] or one or more proteasome inhibitors like Takeda/Millennium's [4502-JP, NR] bortezomib/Velcade or Amgen's [AMGN-Q, NR] carfilzomib/Kyprolis, usually in combination with the corticosteroid dexamethasone) still have so-called minimal residual disease (MRD) that is more easily detected by some sort of biomarker or genetic assay than by visual inspection with CT- or MR-imaging.
- We provided more comprehensive context on the MRD diagnostics market specifically in multiple myeloma standard-of-care in our last Healthcare Weekly, ostensibly in response to the corporate update published by MB-based telomere visualization/interpretation-focused diagnostics firm Telo Genomics (TELO-V, NR) that continues to develop its TeloView platform for multiple diagnostics medical markets, initially with a focus on cancer diagnosis & even more focused on multiple myeloma as a flagship indication. The concept of AI-enabled diagnostic assay development runs parallel to the analysis of the recent history of AI-based drug discovery that forms the basis for the next section in this edition of our Healthcare Weekly (see below)
- The firm is already partnered with the MN-based Mayo Clinic, with the OH-based Cleveland Clinic & with the EU-based University of Athens on testing TeloView's utility in MRD identification. Then as now, we believe that TeloView performance specifically at an interim analysis of the University of Athens study nicely shows that TeloView can both accurately & precisely identify MRD specifically in advanced multiple myeloma patients with an area-under-curve (AUC;

Please see end of report for important disclosures.

a hybrid statistical & graphical measure of the false positive rate & the false negative rate of a diagnostic assay, collectively considered in a single value from a form of analysis called a receiver operating characteristic, or ROC) value of 0.849, in our view quite positive for a cancer diagnostic assay. A perfect test that never misses a patient with MRD & never falsely identifies a patient who does not will generate an AUC value of exactly 1.0; an imperfect test that is no better than random chance will have an AUC of exactly 0.5 (& a test with an AUC of <0.5 is misidentifying a biological marker as being disease-associated when it in fact has no relevance to disease at all – such tests in our experience rarely if ever get to a clinical-stage of development & thus have little-to-no profile in the public domain).

- As a side point, readers not familiar with biostatistics may be wondering where the term ROC came from, as the words receiver & operating & characteristic seems to have no descriptive capacity for disease diagnosis & we would go one step further in stating that the terms are more confusion than illuminating in the service of understanding disease diagnosis & on how to differentiate between a useful test & a useless one. There is a historic justification for the terminology however. The terms collectively considered actually arose during World War II as a concept used by the British Royal Air Force (RAF) to describe its early warning radar system, designed to analyze radar data in the service of identifying enemy aircraft/fighter jets.

Exhibit 2. Personalis' NeXT Dx Platform & The Quarterly Test Volumes Its DNA/RNA Sequencing Platform Is Generating So Far



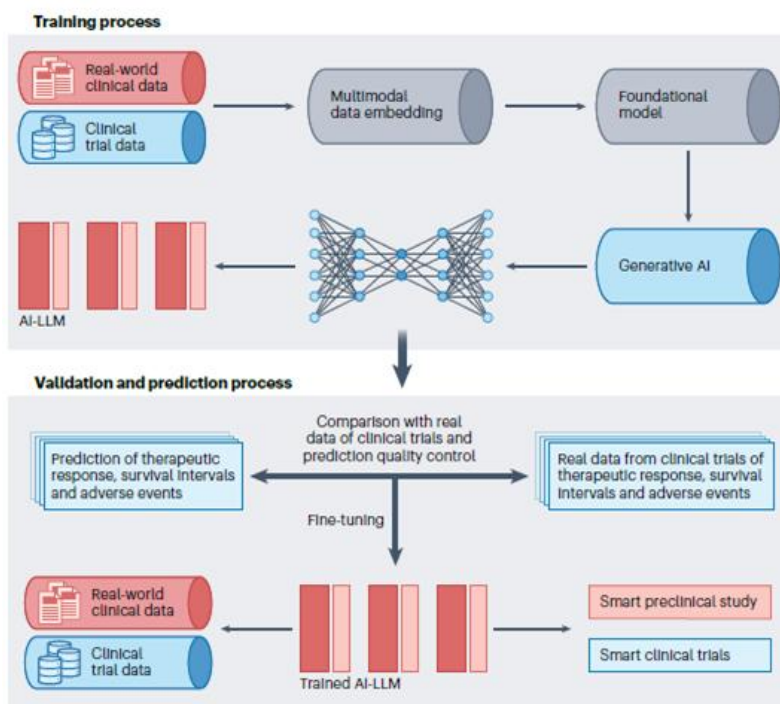
Source: Adapted from Personalis investor presentation (May/26)

- It was recognized in that application that as sensitivity of radar signal detection increased, so too did the likelihood that irrelevant radar signals could emerge that could inaccurately be determined to be aircraft when in fact they were benign airborne objects, say a flock of birds for example. A radar system that deems a flock of birds to be an enemy aircraft is clearly not as specific for enemy aircraft as it needs to be, hence the appreciation through this military application of the key interrelationship between sensitivity & specificity as a general concept, a concept with practical application to disease diagnosis as imaging & molecular detection assays became more sophisticated in the modern scientific era.
- Shifting back to Tempus AI/Personalis, the press release announcing the transaction makes it clear that the two firms were already partners since Nov/23, with Tempus AI making an investment at the time in developing Personalis' NeXT Personal MRD test, a cancer-specific assay that identifies circulating tumor DNA as its source material for identifying post-chemotherapy patients that still may have MRD & thus warrant more vigilant monitoring for disease recurrence potential. The firm's initial applications are for breast & lung cancer, for which multiple biomarker-defined sub-types of disease exist & for which multiple modes of therapy are already FDA-approved. Personalis generated FQ226 revenue of US\$22.4M on 10,384 clinical tests conducted in the period, up from 7,815 tests conducted in FQ126. But going forward, Personalis has published tumor mutational burden data for other cancer forms at recent cancer conferences, including for liver, ovarian, endometrial, kidney, melanoma & colorectal cancer just within the last few months. Prior to the Tempus AI transaction, Personalis was guiding capital markets to expect F2026 revenue of US\$78M-to-US\$80M, an estimate that seems highly conservative based on test volume growth & FQ226 run-rate alone.
- The NeXT Dx platform combines whole genome DNA sequencing with whole transcriptome RNA sequencing & then compares these sequence data not just to each other but also to an AI-generated library of DNA/RNA sequencing data generated for both normal & tumorous breast or lung tissue. Such analysis can thus identify any alterations in DNA copy number or if any tumor-associated DNA insertions/deletions/mutations/fusions (collectively called tumor mutational burden, or TMB) are identifiable in RNA transcripts encoded by such DNA alterations. This approach is conceptually logical but likely complex as a practical data management exercise that we assume required AI capabilities that Tempus AI provides.
- The concept of TMB & how it can be assessed is nicely described in a 2019 review published by Cornell University & University of Bern researchers in the *Journal of Clinical Oncology* that we reviewed as background for the Tempus AI/Personalis transaction. And there are countless peer-reviewed papers describing various elements of tumor mutational burden that can be assimilated into AI analysis, which Tempus AI/Personalis have presumably conducted & continue to do so. At present, there are 401 distinct tumor-associated nucleic acid modifications that form the basis for NeXT Dx analysis, each of which Personalis identifies overtly in its product description, with several literature references published between 2019-to-2022 that support the relevance of the DNA/RNA modifications that NeXT Dx assesses. In its public documents, Personalis indicates that it has a next-generation suite of B-cell & T-cell receptor modifications that it incorporates into its ImmunID NeXT diagnostic platform. Tempus AI itself claims that MRD alone could be a US\$20B cancer diagnostic market on its own, though an estimate this high likely applies to all cancer forms for which residual disease post-therapy is relevant & not just multiple myeloma - justifying in our view Telo's ongoing focus on this market through its existing alliances & independent R&D activities.
- As we described last week, the leader in MRD analysis in multiple myeloma specifically is WA-based Adaptive Biotechnologies (ADPT-Q, NR), which by using its nucleic acid sequencing platform clonoSEQ can identify sequence modifications within the CDR3 regions of the B- & T-cell receptors to identify multiple myeloma patients with MRD. MRD-based laboratory services are a substantial lucrative component of Adaptive's diagnostic operations - 86% of the firm's FQ425 revenue of US\$71.7M & an even higher 95% proportion of FQ126 revenue of US\$70.9M were MRD/multiple myeloma-based & its F2026 full-year MRD revenue guidance is actually a bit conservative just on a FQ126 run-rate basis (US\$260M-to-US\$270M). As we have described many times before in our **Oncolytics Biotech (ONCY-Q, Spec Buy, PT US\$3.00)** commentary, Adaptive was also collaborating with Oncolytics by using its ImmunoSeq T-cell receptor sequencing platform for identifying T-cell clones associated with breast cancer responsiveness to Oncolytics' reovirus formulation pelareorep, specifically in the now-completed AWARE-1 & BRACELET trials.
- The other major competitor in the MRD/multiple myeloma diagnostics space is Euroflow NGF, a next-generation flow cytometry (NGF)-based assay developed by a Netherlands-based research alliance predictably named Euroflow & then developed commercially by the Spain-based private firm Cytognos SL. Cytognos through two separate transactions is

now part of US-based analytical equipment manufacturing/marketing giant Waters Corporation (WAT-NY, NR). Euroflow NGF is described in multiple peer-reviewed studies, including but not limited to a 2023 study published by Kanazawa University-based researchers in the *European Journal of Haematology* & a Jun/26 study published by a Spain-based research consortium in the journal *Hemasphere*.

- The Euroflow consortium was describing flow cytometry as a cancer diagnostic modality in MRD as far back as 2005, when the consortium itself was founded & in its early days during 2006-to-2012 it was actually more focused on identifying flow cytometry-relevant tumor cell surface markers to which fluorescently-labelled mAbs could be bound in identifying leukemia/lymphoma, not yet identifying Euroflow NGF's adaptability to MRD/multiple myeloma until much later. Unlike Adaptive, Waters does not provide much product-specific granularity in its quarterly financial data, so we do not know what Euroflow NGF's quarterly test volume is with any precision
- But in conclusion, we are certainly seeing growing awareness of the utility of molecular tools (of which TeloView's ability to interpret telomere architecture is one) for identifying MRD & recent revenue traction in that realm (Adaptive) & acquisition activity in that same realm (Waters acquisition of BD Biosciences in Feb/26 which itself acquired Euroflow NGF developer Cytognos SL in Feb/22) is evidence of that trend. Telo's market profile will be driven in pending quarters though by its own pipeline advances & thus by its own demonstration of TeloView's comparative utility in disease diagnosis, & not just in multiple myeloma. Founding researcher Sabine Mai has published multiple papers on TeloView, showing how the platform can be useful in other oncology & CNS indications, with encouraging insights into prostate cancer- & Alzheimer's disease-associated telomere modifications that we believe can be leveraged in future commercial/diagnostic applications.

Exhibit 3. Predicting Clinical Responses Through Analysing Historic Clinical Responses Is Of Course Just As Critical To AI Success As All Of The Pharmacologic/Chemical Insights That Came Before

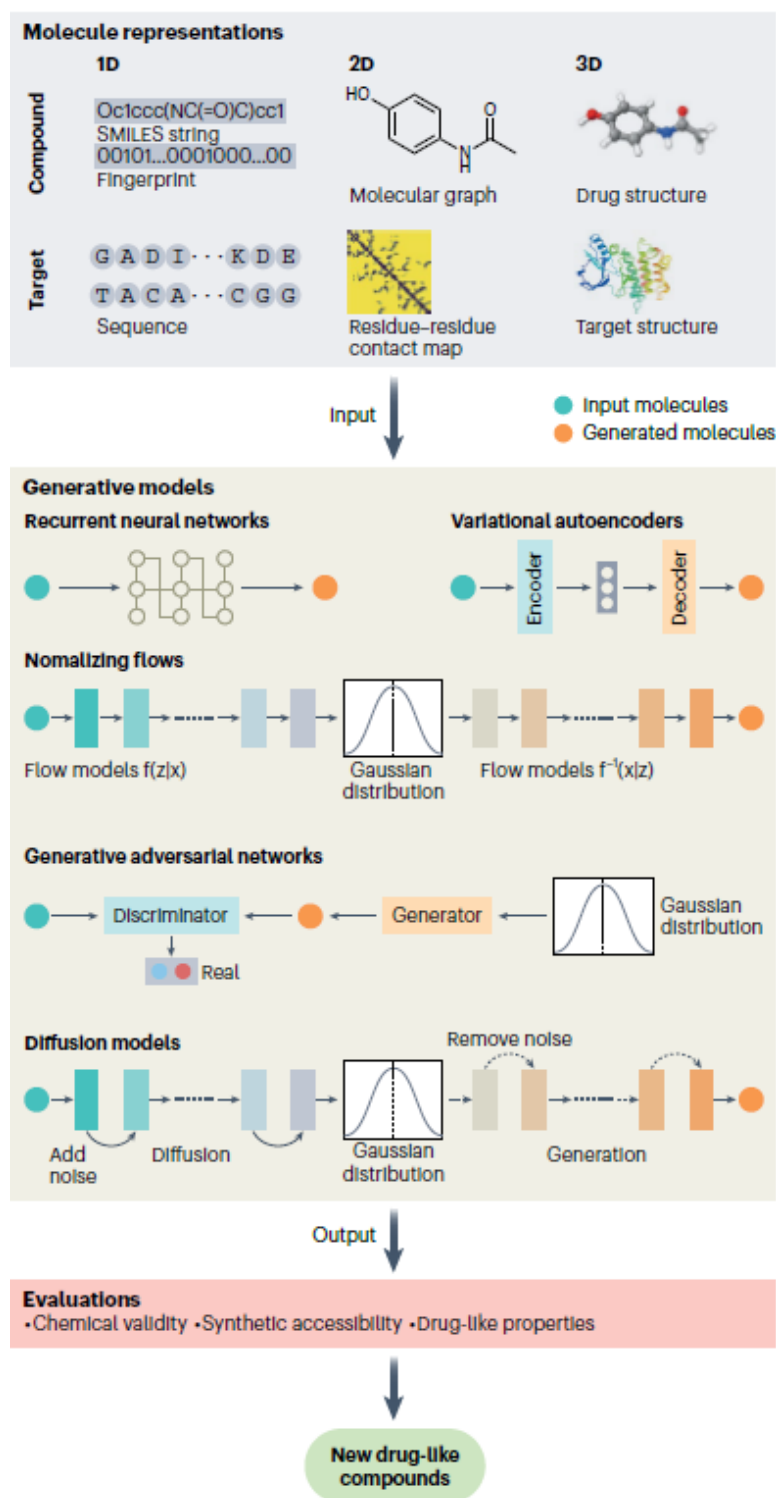


Source: Adapted from *Nature Medicine* (2025). Vol. 31, pp. 45-59

- **AI drug development marches on, not just in early-stage discovery alliances but also in advanced clinical programs that serve to validate AI approaches to both lead molecule & new target identification.** Back in an earlier edition of our Healthcare Weekly that we published back in late April/26, we identified & described several mid-stage small molecules & biologics that were known to have been discovered (or in some cases, their newly-identified biological targets were discovered) using computational AI-based methodologies & that analysis led us to conclude that AI is not just a novelty that will come & go as new drug discovery innovations emerge but is a technological (& in some ways philosophical) approach to drug discovery

that if anything could intensify in coming quarters. That can only happen if early AI-identified drugs/biologics perform well in Phase I-to-III clinical trials & there are several ongoing such trials that give us a basket of evidence to assess AI's relevance in the drug discovery continuum.

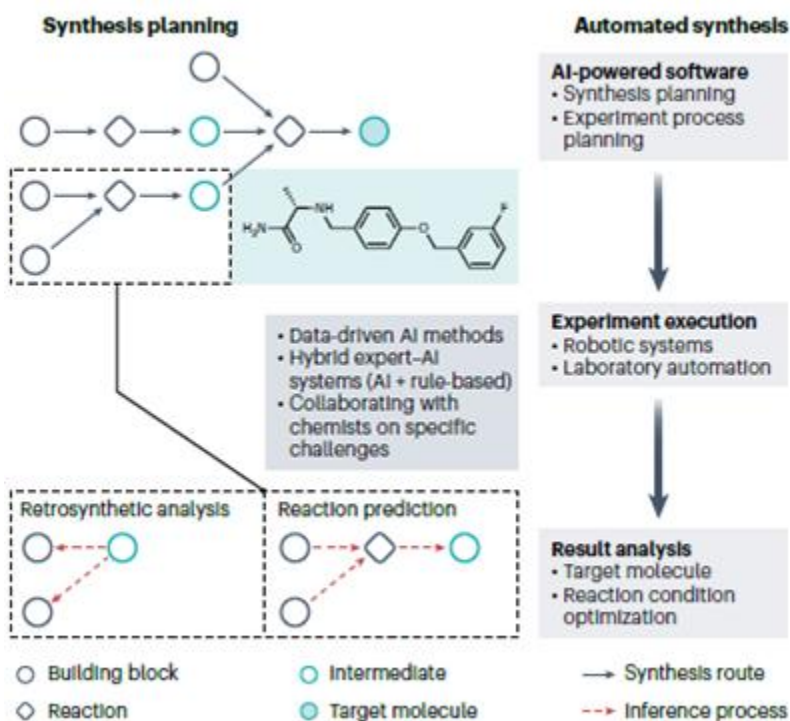
Exhibit 4. Leveraging Neural Networks Is One Approach To AI-Based Drug Discovery/Lead Identification That Has Long Been The Focus Of Computational Chemistry & Its Innovators



Source: Adapted from *Nature Medicine* (2025). Vol. 31, pp. 45-59

- We do not intend to repeat that analysis here – we can send our Apr/26 Healthcare Weekly in pdf form to any interested readers – other than to summarize in tabular form those drugs that we identified at the time & for which clinical testing was active (see Exhibit 8, supplemented by a table of other referenced AI-derived drugs in Exhibit 9). Observe that we have highlighted in blue those clinical programs that have been discontinued since being identified a couple of years ago, showing in these early days of AI-directed drug discovery that AI's batting average is approaching but has not yet achieved perfection.

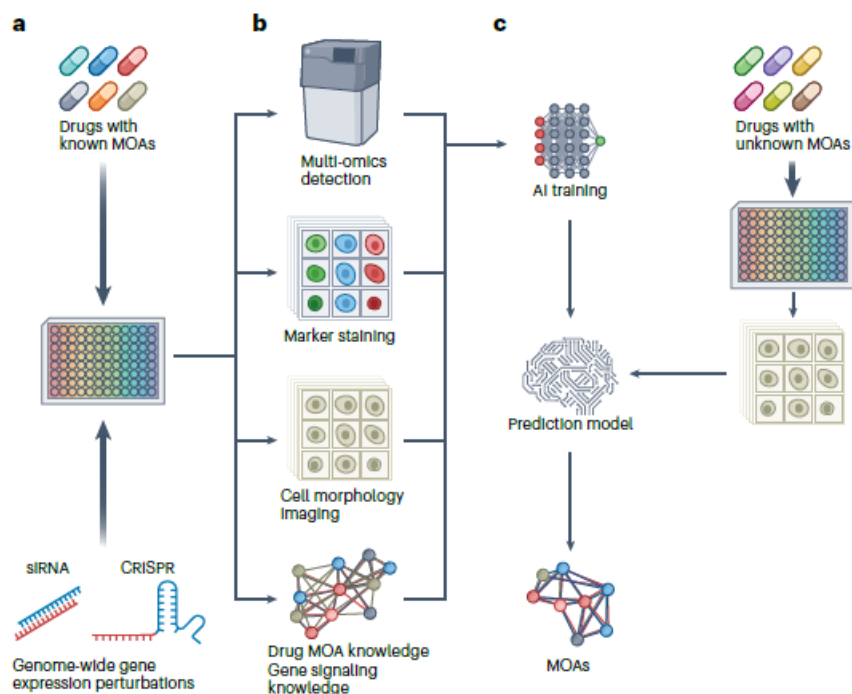
Exhibit 5. A Non-Trivial Component Of The AI Drug Discovery Continuum Is Moving From What Is Theoretically Possible To What Is Synthetically Possible To What Is Practically Achievable



Source: Adapted from *Nature Medicine* (2025). Vol. 31, pp. 45-59

- The data set of failed AI-based drug development programs is far too small to identify any trends or patterns, with two discontinued programs focused on antibody development & two focused on small molecule development, two focused on oncology & the other two focused on infectious disease & an orphan neurology indication (amyotrophic lateral sclerosis, a notoriously challenging disease to target, which we infer just from its limited pharmacopeia that for years was just Sanofi's [SNY-NY, NR] now-genericized benzothiazole drug riluzole/Rilutek, though more recently includes Shionogi/Mitsubishe Tanabe's [4507-JP, NR] pyrazolinone drug edaravone/Radivava & Biogen/Ionis Pharmaceuticals' [BIIB-Q, NR; IONS-Q, NR] the *SOD1* [short for superoxide dismutase-1]-targeted antisense oligonucleotide drug tofersen (BIIB067)/Qalsody) & with no mechanistic overlap that we can discern from this failed clinical data set.
- Herein we continue that analysis by identifying a parallel suite of drugs/biologics in active clinical testing & for which we have some foundational pharmacologic information on which to base a view on their respective prospects. We uncover a few other discontinued AI-inspired clinical programs in our follow-up analysis of the space, though with other programs advancing well & in support of AI's current status as a useful if imperfect drug discovery modality.
- Then as now, we are referencing drugs that were identified in two distinct publications – a May/24 review article published in the journal *Science* by staff writer Derek Lowe & a separate review published in Nov/25 in the *Journal of Medicinal Chemistry* by pharmacology/toxicology researchers at the University of Texas. With that as a preamble, other AI-discovered drugs or biologics that are either in active clinical testing, or were until recently, are as we describe in our commentary below. As our commentary will show, AI-inspired drugs/biologics still encounter Phase II challenges despite prior preclinical/Phase I successes, just as legacy drug development modalities do, but we do expect AI to be increasingly relevant to drug discovery in coming years & for its Phase II/III batting average to improve over time.

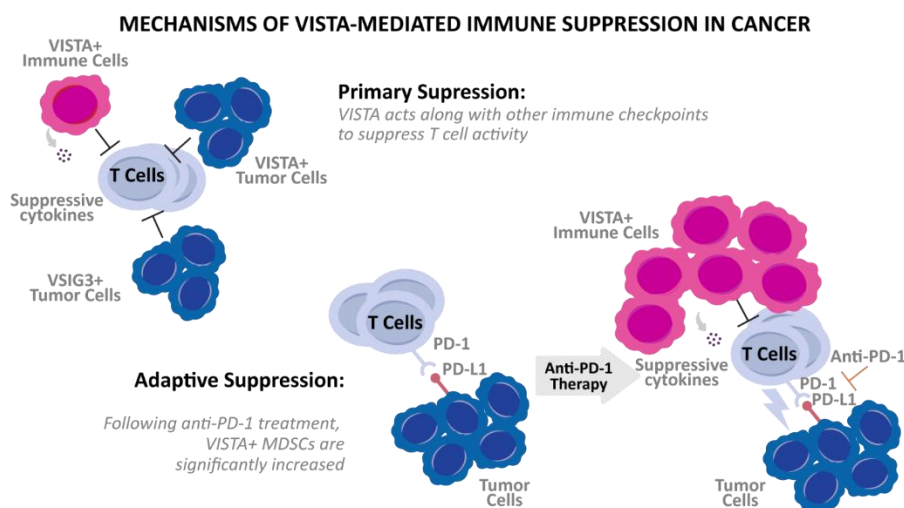
Exhibit 6. Predicting Mechanism Of Action Is Obviously Key To Identifying Feasible Drug Structures, Both To Predict Disease-Relevant Activity & To Predict Side Effect Profile That If Unfavorable Can Be Just As Detrimental To Drug Development



Source: Adapted from *Nature Medicine* (2025). Vol. 31, pp. 45-59

- ♦ **HMBD-002 (Phase II-pending).** This anti-VISTA mAb (VISTA is short for V-domain Ig-suppressor of T-cell activation) completed Phase I/II testing by Singapore-based Hummingbird Biosciences (private) in partnership with Melbourne-based Percheron Therapeutics (PER-ASX, NR) in a 48-patient solid tumor trial completed in late FQ424 that showed no major side effect concerns & so more comprehensive Phase II solid tumor testing, probably in combination with Merck's (MRK-NY, NR) anti-PD1 mAb pembrolizumab/Keytruda as in Phase I testing, is planned to commence some time during FH226. Back in Jun/25, Percheron was granted exclusive worldwide rights to HMBD-002 for which Hummingbird could receive up to US\$290M in downstream development milestones.

Exhibit 7. Proposed Mechanism of Action Of VISTA-Targeted Drugs/Biologics, Of Which HMBD-002 Is One



Source: Hummingbird Bioscience

- ♦ Foundational pharmacology for the mAb was published in 2022 by Hummingbird & collaborators at the national University of Singapore & Stanford University, showing therein that HMBD-002 was able to impede binding of natural ligands to VISTA & in so doing could reduce myeloid cell-derived suppression of T-cell activity while simultaneously impeding neutrophil migration in murine models of immune activation. This activity impeded tumor growth in animal models of colorectal, breast & lung cancer, thus providing clear evidence of preclinical anti-cancer activity through VISTA inhibition, in our view justifying Percheron/Hummingbird's investment in pending Phase II activities indicated above.

Exhibit 8. A Summary Of AI-Discovered Small Molecules & Biologics That Are Or Were In Active Clinical Testing & That We Described In An Apr/26 Edition Of Our Healthcare Weekly

Experimental Drug	Innovator	Ticker	Mechanism of Action	Target Indication	Molecular Details	Develop status	Clinical Details	Timeline to Data	Relevant Partnerships Or AI Platform
ATH-063	Athos Therapeutics	Private	G9A methyl-transferase inhibitor	Ulcerative colitis	Small molecule	Phase II	120-patient (three-month clinical remission rate)	Dec-28	AthosOmics.AI
BEN-8744	Osaka Holdings	2502-JP	Phosphodiesterase-10 inhibitor	Ulcerative colitis	Small molecule	Phase II pending	76-patient Phase I completed in Mar/24	NA	Benevolent AI; data in Jan/25 abstract in <i>J. Crohns & Colitis</i>
BDTX-4933 (S241656)	Black Diamond Therapeutics	BCTX-Q	Braf oncogene inhibitor	Solid tumors	Small molecule	Phase II	554-patient Phase II solid tumor (PK, resp rate, PFS, OS)	Jan-28	Servier (US\$780M alliance in Mar/25)
BDTX-1535 (silevertinib)	Black Diamond Therapeutics	BCTX-Q	EGF receptor inhibitor	Glioblastoma	Small molecule	Phase II	162-patient in unmethylated MGMT patients (PFS, OS)	Mar-28	NA
CEL-383 (ABBV-8736)	Celsius Therapeutics (AbbVie)	ABBV-NY	anti-TREM1 mAb (triggering receptor expressed on myeloid cells-1)	Crohn's disease	Antibody	Phase II	540-patient (3-month endoscopic remission)	Jan-30	AbbVie acquired Celsius in Jun/24 for US\$250M
BAY1905254 (bapotulimab)	Bayer AG	BAYN-DE	anti-ILDR2 mAb (Ig-like domain-containing receptor-2), targets T-cell activity	Head & neck cancer	Antibody	Phase II pending	60-patient Phase I completed in May/24	NA	Not included in Bayer's current pharmacology pipeline
HFB301001 (nuvustotug)	HiFiBio Therapeutics	Private	anto-OX40/CD134 mAb (amplifies T-cell mediated immunity)	Solid tumors	Antibody	Discont	31 patient Phase I terminated in May/24	NA	Preclinical data published in Mar/26 in <i>Journal for ImmunoTher of Cancer</i>
HFB200301 (emunkitug)	HiFiBio Therapeutics	Private	anti-TNFR2 mAb (tumor necrosis factor receptor-2)	Solid tumors	Antibody	Phase I/II	72-patient Phase II (resp rate, PFS, duration of response)	Dec-26	Tested with BeOne Medicine GmbH's anti-PD1 mAb tislelizumab
HFB200603	HiFiBio Therapeutics	Private	anti-BTLA mAb (B- & T-lymphocyte attenuator)	Solid tumors	Antibody	Phase I/II	83-patient Phase II (resp rate, PFS, duration of response)	Dec-26	Also tested with BeOne Medicine GmbH's anti-PD1 mAb tislelizumab
HST-1011	HotSpot Therapeutics	Private	CBL-B inhibitor (an E3 ubiquitin ligase, protein degradation)	Solid tumors	Small molecule	Phase I/II	77-patient Phase II (resp rate, PFS, duration of response)	Dec-26	Tested with Regeneron's anti-PD1 mAb cemiplimab
HMBD-001	Hummingbird Bioscience	Private	anti-HER3 mAb (tumor-associated EGFr variant)	Squamous cell canc (lung, H&N, esoph)	Antibody	Phase II	398-patient (PK, resp rate, PFS)	Dec-27	Combining with cetuximab & docetaxel
REC-3964	Recursion Pharmaceuticals	RXRQ-Q	Diazepinedione analog (targets <i>C. difficile</i> toxin B)	<i>Clostridium difficile</i> GI infection	Small molecule	Discont	First-in-human testing terminated in May/25	NA	AI platform identifies new pipeline in REC-4881, REC-617, REC-1245
VRG-50635	Verge Labs	Private	Phosphoinositide-3-kinase inhibitor	Amyotrophic lateral sclerosis (ALS)	Small molecule	Discont	54-patient Phase I terminated in Jul/25	NA	Focused on partnering its AI platform in CNS disorders, Eli Lilly-backed

Source: Leede Financial (Healthcare Weekly, Apr 24/26 edition), company reports, *Science* (2024; author Derek Lowe)

- ♦ Interestingly, in a Jul/25 press release from Percheron, the firm summarized new preclinical data showing that HMBD-002 in combination with radiotherapy was effective at eradicating head & neck cancer in a murine model of that cancer form. This activity was exhibited both on tumor response & extended survival of test animals. Those data are not yet published in peer-reviewed form to our knowledge but they do extend the suite of VISTA-expressing solid tumor forms (a list that presumably includes colorectal, lung, breast & now head & neck cancer) that could be

targeted in Phase II; neither Hummingbird nor Percheron have provided insights into Phase II clinical trial design just yet, but presumably such details are pending. HMBD-002 is Percheron's only pipeline asset.

- Competitive VISTA-targeted therapies that are themselves in early-stage Phase I/II cancer testing include MA-based Curis (CURI-NS, NR) & Aurigene Oncology's (now part of Dr. Reddy's Laboratories [REDY-NS, NR]) orally-active small-molecule checkpoint inhibitor CA-170 (a 71-patient Phase I advanced tumor trial was completed in F2020), Curis/ImmuNext's zirconium-89-labelled anti-VISTA mAb CI-8993 (originally called onvatilimab/JNJ-61610588 when Janssen Biotech (JNJ-NY, NR) was developing the drug; data from a 26-patient Phase I trial concluded during FQ223) & FL-based Kineta/TuHura Biosciences' (HURA-Q, NR) anti-VISTA mAb trovostobart/KVA12123 (now called TBS-2025, for which an IND was filed in Jun/26, intending to test the mAb in acute myeloid leukemia).

Exhibit 9. A Summary Of AI-Discovered Small Molecules & Biologics That Are Separately Described In The Chemical Literature

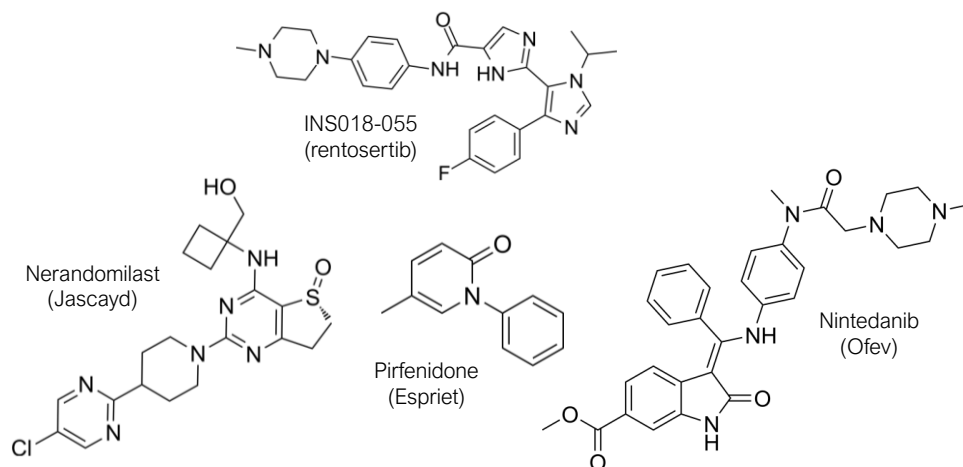
Experimental Drug	Innovator	Ticker	Mechanism of Action	Target Indication	Molecular Details	Develop status	Clinical Details	Timeline to Data	Relevant Partnerships Or AI Platform
AI-assisted repurposed drugs									
Baricitinib (Olumiant)	Benevolent AI/ Eli Lilly	LLY-NY	JAK1/2 inhibition	SaRS-CoV2 infect, rheum arthritis	Small molecule	Approved	Six Phase II/III RA studies totalling 2,546 patients	NA	Benevolent AI Platform
AI-designed de novo									
DSP-1181	Exscientia (Recursion Pharma)/ Sumitomo	RXRX-Q, 8053-JP	Serotonin 5-HT1A receptor agonist	Obsessive compulsive disorder (OCD)	Small molecule	Discont	Phase I terminated	NA	Described in 2021 paper in <i>Physiological Reviews</i> ; Exscientia acquired by Recursion in Nov/24
Halicin	MIT/Broad Institute	Private	Thiadiazole; disrupts proton-motive force in bacterial membrane, reduces ATP synth	Antibiotic-resistant infection	Small molecule	Phase I pending	Preclinical activity against drug resistant bacterial strains	NA	Described in 2025 in <i>Antibiotics (Basel)</i>
ISM001-055/ rentosertib	InSilico Medicine	3696-HK	TNIK inhibitor (Traf2 & NCK-interacting kinase)	Idiopathic pulmonary fibrosis	Small molecule	Phase III	320-patient (FEV, lung fibrosis impact at one-year follow-up)	Dec-29	Described in 2025 in <i>Nature Biotechnology</i>
AI-designed de novo									
EXS-21546	Exscientia (Recursion Pharma)	RXRX-Q	Adenosine A2A receptor antagonist	Solid tumors	Small molecule	Discont	64-Phase I completed in Q222; Phase II solid tumor trial terminated	NA	Exscientia acquired by Recursion in Nov/24
ATM-3507	Numerion Labs (Atom-wise, Univ of Tor spin-out)	Private	Tropomyosin isoforms 3.1 & 3.2 inhibitor, alters B-cell actin architecture	Multiple sclerosis	Small molecule	Pending	Preclinical data originally published in 2017 in <i>Molecular Cancer Therapeutics</i>	NA	Described in Nov/25 in <i>Front Immunol</i> , Sanofi ptrnship in Aug/22, APEX platform devel with Nvidia
DSP-0038	Exscientia (Recursion Pharma), Sumitomo	RXRX-Q, 8053-JP	Serotonin 5-HT2A recept antagonist, 5-HT1A receptor agonist	Alzheimer's disease psychosis	Small molecule	Phase I	In Sumitomo's Psychiatry & Neurology pipeline	NA	Exscientia acquired by Recursion in Nov/24
IAMA-6/ ARN23746	Iktos/ Almirall SA	IKTO-Q; ALM-MC	Sodium-potassium-chloride co-transporter-1 (NKCC1) inhibitor	Dermatology	Small molecule	Phase II pending	72-patient Phase I (Q424); preclin data (<i>ACS Pharmacol Transl Sci</i> , 2023)	NA	Makya 2.0 is AI/robotics platform; Iktos partnered with Servier & Pierre Fabre Labs in Jan/26
BEN-2293	Benevolent AI	Private	Pan-TRK (tropomyosin receptor kinase) antagonist	Atopic dermatitis	Small molecule	Phase I/II completed	123-patient (one-month EASI scores, NRS for pruritis, PK)	NA	Benevolent AI; described in 2022 review in <i>Amer J Clinical Dermatology</i>

Source: Leede Financial, company reports, adapted from *Pharmaceuticals (2025)*. Vol. 18, pp. 1271-1299

- INS018-055/rentosertib (Phase III testing ongoing).** This small molecule inhibits the signaling kinase TNIK, short for Traf2 & NCK-interacting protein kinase, an enzyme that adds a phosphate group to other proteins & in so doing regulating the activity of signalling pathways that include it in its cascade (in this case, regulating transcription of various proteins that influence cell growth or that influence the cytoskeleton architecture of cells, with notable impact on lung scarring & thus on pulmonary fibrosis). The role of TNIK inhibition in mitigating pulmonary fibrosis, with INS018-055/rentosertib specifically featured in that analysis, is described in a Jan/25 paper published in *Nature Biotechnology* that we reviewed for this commentary.

- ♦ The drug was discovered by MA- & Hong Kong-based InSilico Medicine's [3696-HK, NR] that has been the subject of multiple points of interest in our legacy AI commentary, most recently with its US\$177M neurology-focused AI-based drug discovery relationship with China-based China Medical System Holdings (867-HK- NR) that we described last week, with its US\$2.75B blockbuster alliance with Eli Lilly [LLY-NY, NR] announced in Mar/26 & with its US\$888M oncology-focused alliance with France-based private pharma firm Servier announced in Jan/26. InSilico's core receptor identification platform PandaOmics/Biology42 & its novel molecule identification platform Chemistry42 were presumably relevant in identifying INS018-055/rentosertib for future lung fibrosis testing.
- ♦ And InSilico's pace of new alliance consummation continued with its new US\$2.5B relationship announced earlier this month with Taiwan-based Bora Pharmaceuticals (6472-TW, NR), with the associated press release mostly a stream of motherhood statements about AI's potential but without mentioning any specific target indications or molecular mechanisms on which the new partners will focus. The InSilico-Bora relationship is probably more focused on optimizing the interrelationship between AI drug discovery & the practical manufacturing consequences that flow from that discovery; Bora says as much in its own press release on the alliance.
- ♦ Accordingly, InSilico is testing INS018-055/rentosertib in a 320-patient Phase III idiopathic pulmonary fibrosis trial for which one-year impact on lung function (forced expiratory volume & CT-confirmed reduction in lung fibrosis) are projected to be available by end-of-F2029. Back when we were following Liminal Biosciences (now private) & focused on the firm's small-molecule drug PBI-4050 as a lung fibrosis-reversing agent, the competitive landscape in idiopathic pulmonary fibrosis was dominated by Roche's (ROG-SW, NR) anti-fibrotic drug pirfenidone/Espriet that it no longer sells (divesting marketing rights to Cayman Islands-based Legacy Pharma [private] in Feb/25 after acquiring pirfenidone's innovator InterMune for US\$8.3B back in Aug/14; core patents expired on the drug in 2022) & by Boehringer Ingelheim's (private) triple angiokinase-inhibiting drug nintedanib/Ofev (F2025 sales €3.8B) & its more recently-launched phosphodiesterase-4B inhibitor nerandomilast/Jascayd (FDA-approved in Oct/25, EMA-approved this month).

Exhibit 10. Molecular Structures Of AI-Discovered TNIK-Inhibiting INS018-055/Rentosertib & Of Other Mechanistically-Distinct FDA-Approved Idiopathic Pulmonary Fibrosis Drugs That Came Before it



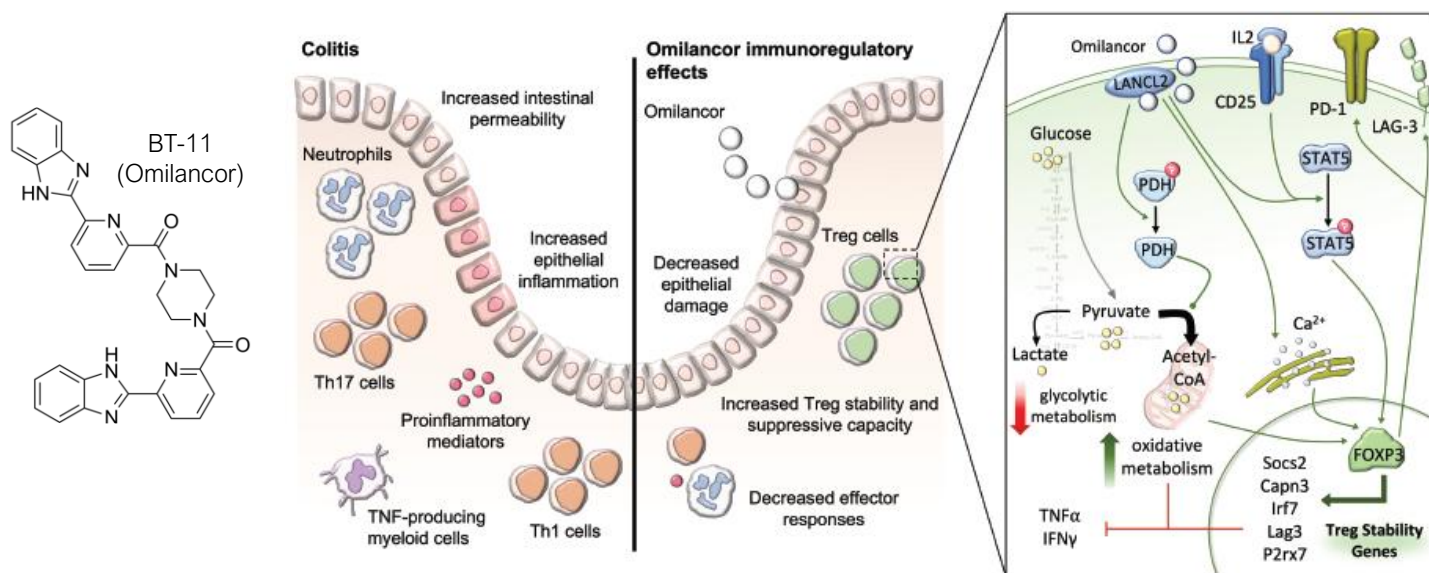
Source: MedChemExpress

- ♦ **BT-11/Omilancor (Phase III-pending).** Also called BT-11 in its early development days by VA-based private drug developer NImmune Biopharma, this orally-active small-molecule activator of the LANCL2 protein (short for lanthionine synthetase cyclase-like receptor-2), a 450-amino acid mitochondrial receptor protein that regulates helper-T-cell function. Omilancor/BT-11 underwent Phase II testing in a 198-patient ulcerative colitis trial that concluded during mid-F2021, with favorable description of the drug's prospects in that indication published in 2024 in the journal *Inflammatory Bowel Disease*.
- ♦ The drug was undergoing clinical testing in a 27-patient Phase II Crohn's disease trial that was withdrawn in 2022, despite which the drug is still identified in NImmune Biopharma's pipeline as being a Phase II-stage ulcerative colitis

asset. Indeed, there is a published retraction of Phase II omilancor data that appears in *Inflammatory Bowel Disease* in Apr/22 that undoubtedly stalled clinical testing until recently. But that said, the drug is featured prominently in the firm's July/26 investor presentation in which its lead indication is still ulcerative colitis (with Crohn's disease not far behind) for which a NDA filing is anticipated in F2027.

- On that theme, Nimmune Biopharma proposes in the investor presentation to enroll 810 patients in two distinct Phase III ulcerative colitis trials testing a single 440-mg oral omilancor/BT-11 dosage strength & for which primary endpoints will be clinical remission both at three- & twelve-month follow-up, as measured by endoscopically-confirmed mucosal healing. Study design assumes a placebo remission rate of 12%-to-14% & an omilancor/BT-11 clinical remission rate at least twice that value. According to the July/26 presentation, omilancor/BT-11 was identified using Nimmune Biopharma's Titan-X Precision Medicine AI platform that incorporated data from gene expression profiling of colonic biopsy samples from ulcerative colitis patients.
- We do not cover Nimmune Biopharma (it is not yet publicly-traded though it speaks to its desire to be so in the July/26 presentation referenced above) & thus are not intimately familiar with omilancor/BT-11's development history, so we were surprised to see a plethora of clinical data provided in the July/26 presentation that we had not seen before in peer-reviewed form. In one 50-patient ulcerative colitis study presented near the middle of the presentation, 30.4% of omilancor/BT-11-treated patients (seven of twenty-three evaluable subject) are shown to experience clinical remission at some point during follow-up as compared to only 3.7% of placebo patients (one in twenty-seven), with up-regulation of immune cell function more prevalent in drug-treated patients, as manifested for example in a reversal of depletion of regulatory T-cells that is commonly associated with refractory disease.

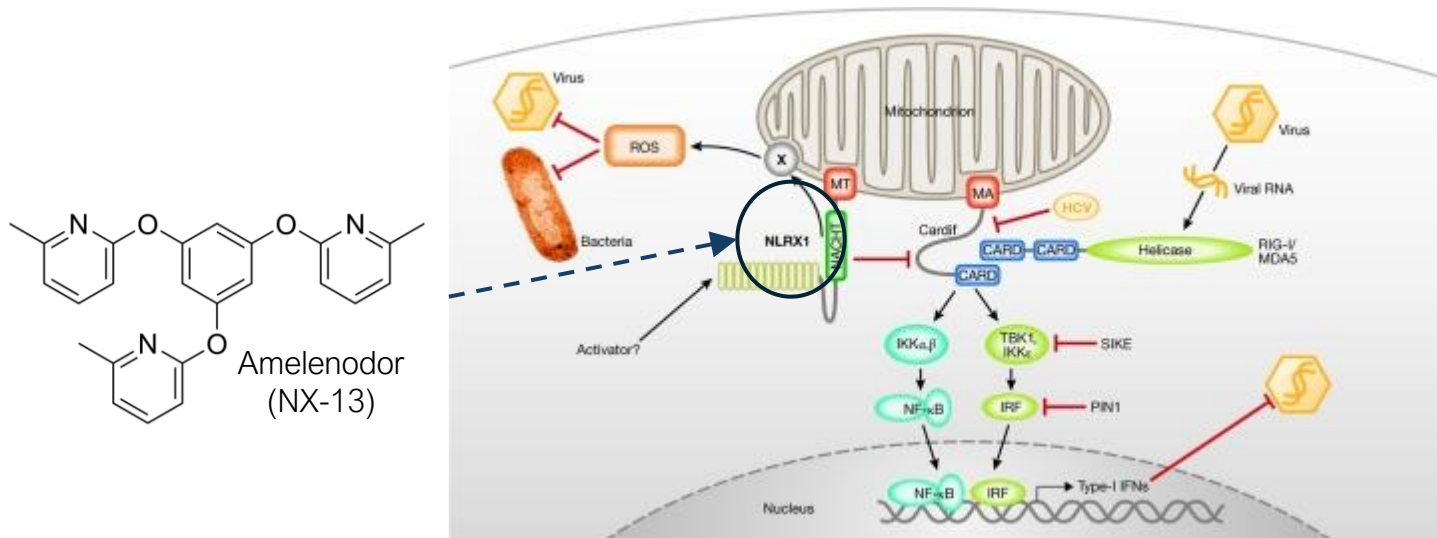
Exhibit 11. Proposed Mechanism For How BT-11/Omilancor Can Mitigate Ulcerative Colitis Or Crohn's Disease Symptoms Through Pathways Mediated By The Mitochondrial LANCL2 Receptor



Source: MedChemExpress; *Inflammatory Bowel Disease* (2024). Vol. 30, pp. 671-680

- NX-13/amelenodor (discontinued).** NX-13/amelenodor is a small-molecule NLRX1 (short for nucleotide binding/oligomerization domain-like receptor family member X1, a seminal protein in a well-characterized innate immunity pathway) agonist drug that was developed by AbbVie/Landos Biopharma [ABBV-NY, NR] that was targeting ulcerative colitis until an 81-patient Phase II ulcerative colitis trial was discontinued in 2025. A 39-patient Phase I trial was completed previously in late F2022 without incident, with data published in May/24 in the *Journal of Crohn's & Colitis* so there were no major alarm bells ringing on putative clinical efficacy arising from prior preclinical/Phase I testing, showing us as so many drug programs do that clinical efficacy can be challenging to predict, even with AI tools at hand.

Exhibit 12. NX-13/Amelenodor Did Not Perform To Expectations In A Phase II Ulcerative Colitis Study, Despite Strong Evidence Of Preclinical/Phase I Activity & Impact On NLRX1-Mediated Anti-Inflammatory Pathways

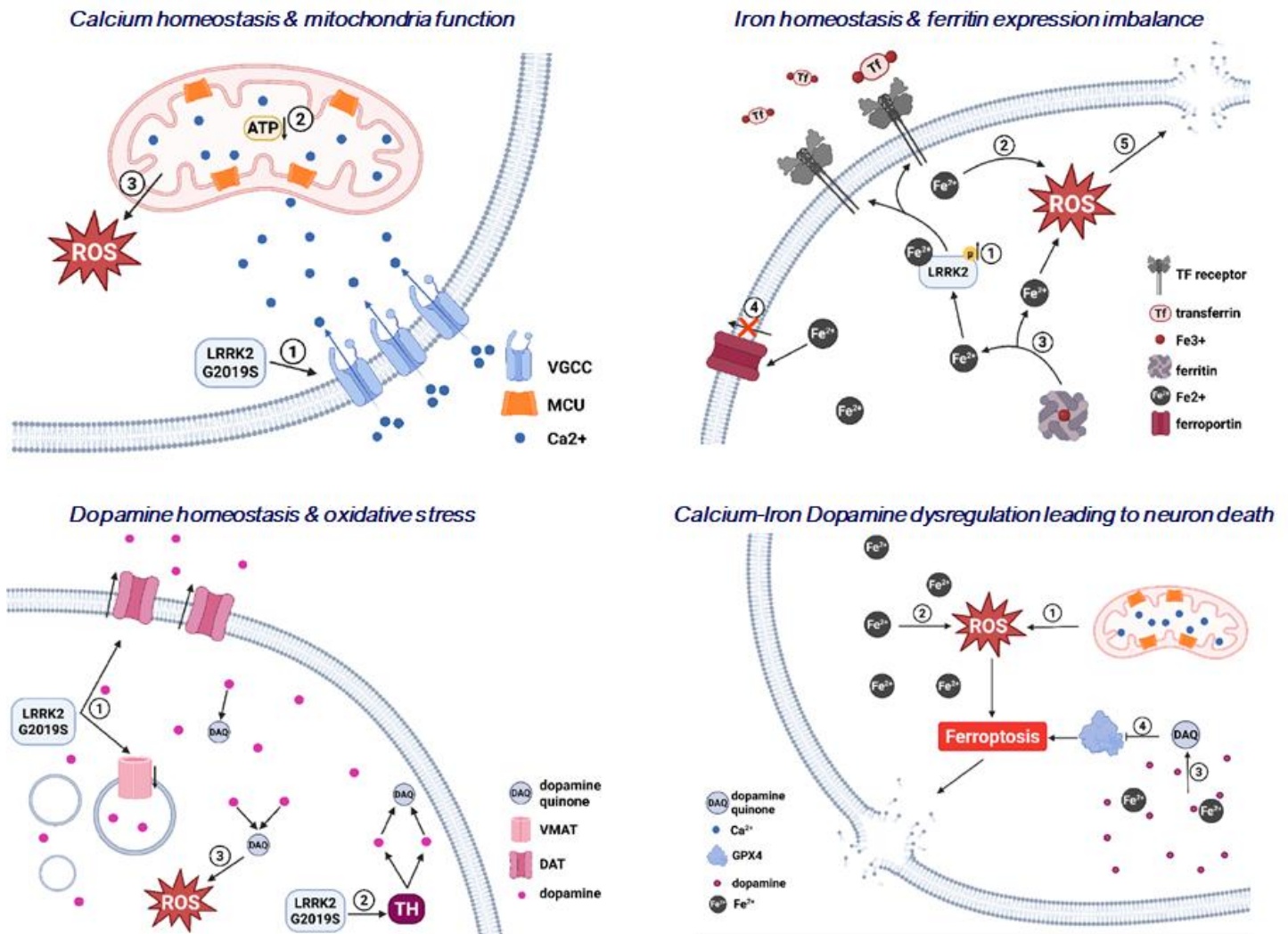


Source: MedChemExpress; *EMBO Reports* (2008). Vol. 9, pp. 243-246

- BT-104/NIM-1324 (Phase II-pending).** BT-104/NIM-1324 is a small-molecule drug that like BT-11/omilancorin described above is also a LANCL2 activator & also developed by Nimmune Biotech, while targeting rheumatoid arthritis & lupus. There are two seminal peer-reviewed papers that describe BT-104/NIM-1324's pharmacologic action, the earliest of which was published in Nov/24 in the *Journal of Immunology*, showing therein that activation of the lanthionine synthetase C-like 2 (LANCL2) protein by BT-104/NIM-1324 mitigated a number of immunological triggers of inflammation, including reduction in so-called hypocomplementemia (low release of complement proteins), reduced kidney histopathology scores & reduces circulating levels of pro-inflammatory cytokines, including those that are responsive to interferon expression while modulating helper T-cell function & enhancing regulatory T-cell activity in the process. Similar to omilancor/BT-11, BT-104/NIM-1324 was discovered using Nimmune Biopharma's Titan-X Precision Medicine AI platform using gene expression profiling data of colonic biopsy samples from ulcerative colitis/Crohn's patients.
- Specific immunologically-active proteins that BT-104/NIM-1324 could reduce in circulation include interferon-alpha, interleukin-6 & interleukin-8, all of which are pro-inflammatory markers that if reduced systemically could mitigate emergence of autoimmune disease symptoms, which Nimmune Biotech is actively exploring. The other paper of interest to us was published in 2025 in the journal *Clinical & Translational Science*, featuring data from a 57-patient Phase I study that concluded by FQ222 & established a maximum tolerated dose for the drug of at least 1,500-mg daily (which preclinical animal models of lupus essentially predicted by establishing a maximum efficacious dose of 20-mg/kg/day in those animals, corresponding to 1,500-mg in a 75-kg patient) while being able to upregulate LANCL2 & stimulate transcription of key inflammatory biomarkers at far lower dosage strengths of as low as 250-mg daily.
- Interestingly, Nimmune Biotech's clinical priorities for BT-104/NIM-1324 shifted in recent years to ulcerative colitis & Crohn's disease, reporting new Phase I data in support of oral dosing in irritable bowel syndrome in May/26 at the annual Digestive Disease Week conference. The firm's scientific team announced prior to that conference that irritable bowel syndrome was now BT-104/NIM-1324's lead indication, with rheumatoid arthritis, lupus & psoriasis now established as secondary indications pending available capital. As of this writing, BT-104/NIM-1324's molecular structure is not formally published in either of the two peer-reviewed papers cited above. We do not see any active BT-104/NIM-1324 clinical trials described in the US NIH's clinical database but we assume that Phase II irritable bowel syndrome testing is pending.

- ♦ **NEU-411 (Phase II testing ongoing).** NEU-411 is a small-molecule LRRK2-inhibiting drug (LRRK2 is short for leucine-rich repeat kinase-2) that was developed by CA-based precision medicine firm Neuron23 [private] that is targeting early Parkinson's disease in the 150-patient NEULARK trial. Primary completion of the trial is expected by late FQ427 & formal study completion is scheduled to transpire by mid-F2028. LRRK2 was shown in prior studies to exhibited elevated kinase activity in Parkinson's patients, usually from mutations in the *LRRK2* gene that are identifiable in about 2% of Parkinson's patients.

Exhibit 13. Foundational Biology By Which LRRK2 Hyperactivity Leads To Neuronal Cell Death In Parkinson's Disease



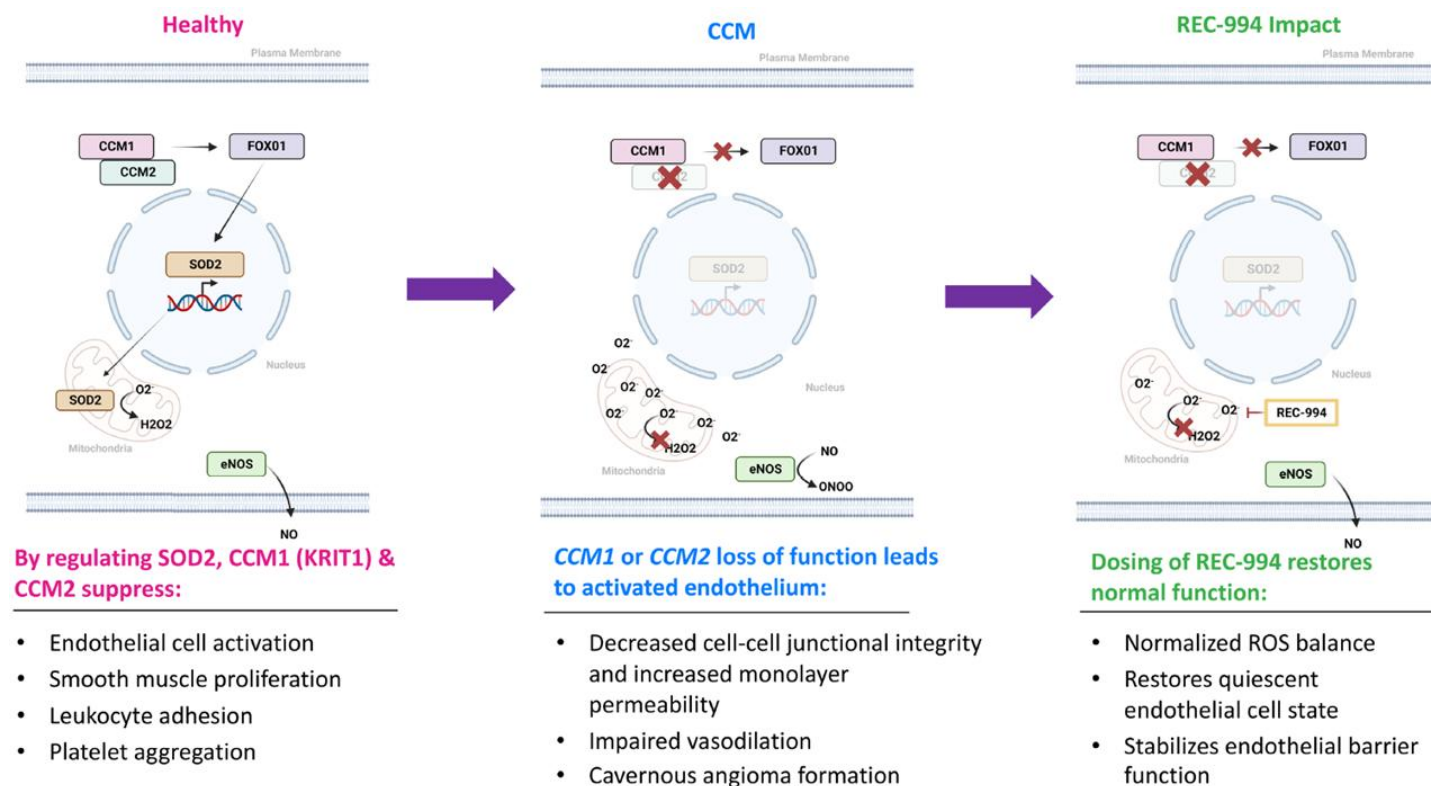
Source: Adapted from *Acta Neurobiologiae Experimentalis* (2026). Vol. 86, pp. 93-108

- ♦ Accordingly, Neuron23 will be using DNA-based diagnostic assays to identify patients with elevated mutation-harboring LRRK2 activity & thus use this assay as one of its screening filters for NEULARK enrollment. Common mutations include but are not limited to a glycine-to-serine amino acid substitution at position #2019 & a separate arginine-to-glycine substitution at position #1441 in LRRK2's amino acid sequence. The primary endpoint in NEULARK will be impact at one-year follow-up on the Roche digital biomarker score as compared to placebo, with a key secondary endpoint being changes from baseline in the so-called Movement Disorder Society's Unified Parkinson's Disease Rating Scale (MDS-UPDRS) over the same time period
- ♦ Recall that Parkinson's disease is separately characterized in the medical literature as being influenced by misfolding of the protein alpha-synuclein, an observation that MA-based ProMIS Neurosciences (PMN-Q, Spec Buy, PT US\$46.00) is leveraging with its preclinical-stage anti-alpha synuclein mAb PMN442. This mAb was raised

against synthetic cyclic peptide antigens that mimic conformational epitopes that are only accessible to mAb binding in misfolded alpha-synuclein & not in alpha-synuclein in its naturally active form.

- ♦ **REC-994/tempol (discontinued).** REC-994/tempol is a small-molecule nitroxide-based scavenger for superoxide free radicals inside cells & tissues & through that activity is thought to be able to mitigate symptoms of diseases associated with superoxide overproduction, an example of which is the brain disorder cerebral cavernous malformation. Indeed, REC-994 was tested in a Phase I study that was published in 2024 in the journal *Pharmacology Research & Perspectives*, showing in that 84-patient single-ascending & multiple-ascending dose trial that the drug engendered no major adverse events with ten-day duration once-daily dosing.
- ♦ The aforementioned disease, cerebral cavernous malformation, is a vascular disease in which small vessels in the brain & spinal cord experience damage to the endothelial cells lining those vessels. By becoming damaged, the disease leads to a suite of CNS symptoms that include headaches, seizures, cognitive impairment & higher risk of hemorrhagic stroke. The disease has overall prevalence of about 15 cases per 100,000 population (or about 360,000 patients combined in the US & western Europe) according to epidemiology data published in the Orphanet database that the above 2024 paper cites in its introduction.

Exhibit 14. Proposed Mode Of Action For REC-994 In Scavenging Superoxide Radicals (So-Called Reactive Oxygen Species, Or ROS) In Blood Vessel Endothelial Cells Did Not Unfortunately Translate Into Phase II Success



Source: Adapted from *Pharmacy & Research Perspectives* (2024). Vol. 12, pp. e1200-1212

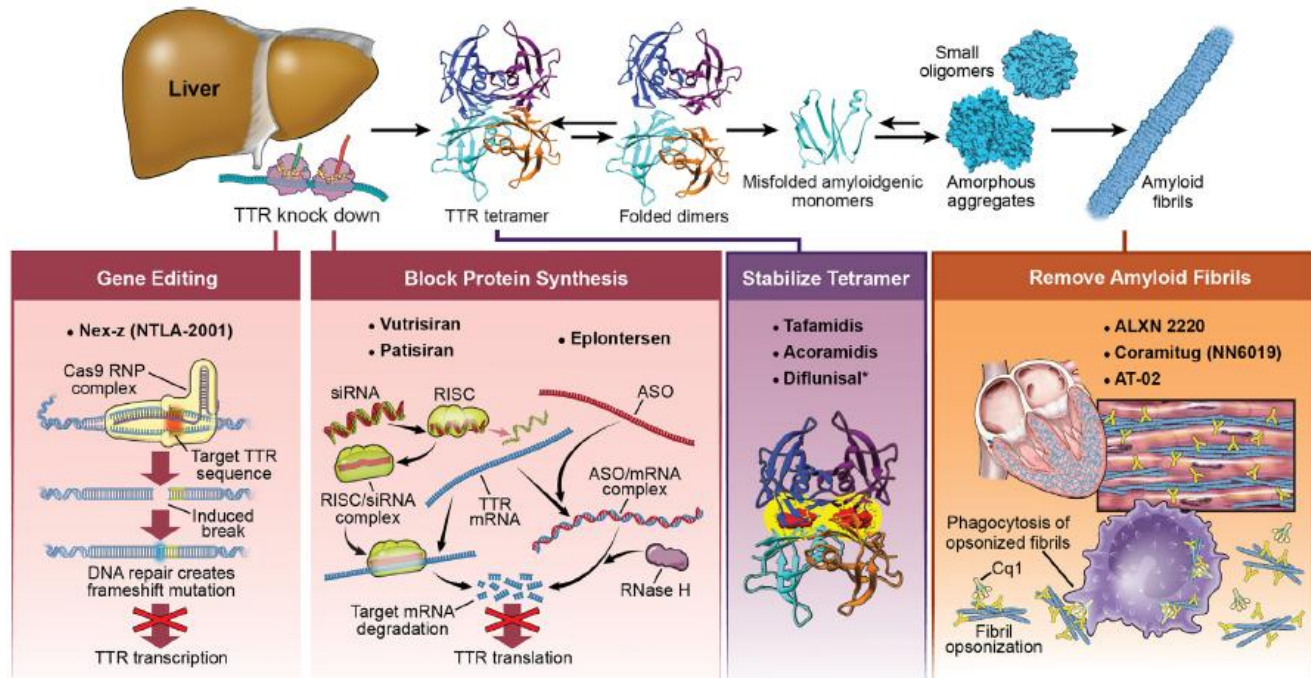
- ♦ UT-based innovator Recursion (RXRX-Q, NR) has already reported positive Phase II cerebral cavernous malformation data in Sept/24 from the 62-patient SYCAMORE trial, showing therein that at the higher of two dosage strengths tested (400-mg once-daily), REC-994 was able to reduce the volume of MR-confirmed disease associated lesions in the brain of diseased patients without incurring any notable side effects over the one-year follow-up period of the trial. Unfortunately, two-year follow-up data on patient self-report as measured by the Modified Rankin Scale & the SymptoMScreen Score & the CCM Health Index were not favorable & the SYCAMORE trial was discontinued & subsequently out-licensed to the philanthropic group Alliance To Cure Cavernous Malformation.

- ♦ Because Recursion is overtly focused on using its Recursion Operating System to drive its AI-enabled drug discovery activities, the discontinuation of REC-994 is best considered at this point in Recursion's pipeline evolution to be a crevice & not a canyon in its path to successful drug development but that sentiment will be tested by other ongoing clinical programs that include:
 - A Phase I/II familial adenomatous polyposis trial (the 67-patient TUPELO trial; data by Q327) testing mitogen-activated kinases 1 & 2 (MEK1/2) inhibitor REC-4881.
 - A Phase I/II solid tumor/ovarian cancer-biased trial (the 230-patient ELUCIDATE trial; data by mid-2028) testing cyclin-dependent kinase-7 (CDK7) inhibitor REC-617 (also called GTAEXS617).
 - A Phase I/II solid tumor & lymphoma trial (the 170-patient DAHLIA trial; data by end-of-2028) testing splicing factor RNA-binding protein-39-targeted (RBM39 degrader) REC-1245.
 - A Phase I B-cell malignancy chronic lymphocytic leukemia-biased trial (the 85-patient EXCELERIZE trial; data by end-of-2028) testing mucosa-associated lymphoid tissue lymphoma translocation protein-1 (MALT1) inhibitor REC-3565 (also called EXS73565).
 - Lastly, a Phase I solid tumor small cell lung cancer- & neuroendocrine tumor-biased trial (the 40-patient ENLYGHT trial; data by Q129) testing lysine-specific histone demethylase-1 (KDM1A, also called LSD1) inhibitor REC-4539 (also called EXS74539).
- **Dyne Therapeutics (DYN-Q, NR) announced FDA acceptance of its BLA for zeleciment rostudirsen** (z-rostudirsen, DYNE-251) for the treatment of DMD amenable to exon 51 skipping, with Priority Review granted & a PDUFA target action date pending in late Jan/27. The submission seeks accelerated approval using dystrophin expression as a surrogate endpoint. Concurrently, Dyne priced a substantial equity offering recently, raising US\$375M in new growth capital, ostensibly to fund pipeline activities in DMD therapy development. The firm's pipeline includes not just z-rostudirsen but also the analogous RNA-based drug z-basivarsen that is targeting a distinct muscular disorder called myotonic dystrophy type-1 (DM1) & for which Phase III testing in the HARMONIA trial commenced in Mar/26.
 - Z-rostudirsen is an RNA-based therapy based on a form of stabilizing chemistry called phosphorodiamidate morpholino oligomer (PMO) conjugation, with a transferrin receptor-1 (TfR1)-targeted antigen-binding fragment (Fab) attached to it. TfR1 is highly expressed on skeletal muscle & CNS cell surfaces, hence its relevance as a targeting modality in DMD. Dyne's proprietary FORCE platform leverages TfR1-mediated uptake to overcome the well-documented delivery limitations of naked PMOs in muscle tissue. Upon internalization, the PMO induces exon 51 skipping in the dystrophin pre-mRNA, restoring the reading frame & enabling production of a near-full-length, internally truncated but functional dystrophin protein (Desjardins & coworkers, *Nucleic Acids Research*, 2024).
 - The Fab-PMO conjugate architecture is designed to improve biodistribution to muscle relative to unconjugated PMOs, which suffer from rapid renal clearance & limited cellular uptake; preclinical data in mdx mice demonstrated dose-dependent dystrophin restoration reaching 51-90% of wild-type levels across multiple muscle groups following a single dose, substantially exceeding levels achieved by naked PMO. Avidity Biosciences (ticker was RNA-Q, NR, since acquired by Novartis [NVS-NY, NR] in Nov/25) took this same approach.
 - The BLA is supported by data from the registrational expansion cohort (REC) of the Phase I/2 DELIVER trial, a global, randomized, placebo-controlled, double-blind study in 32 ambulant & non-ambulant boys with exon 51-amenable DMD aged 4 to 16 years. At the 20 mg/kg Q4W registrational dose, DELIVER met its primary endpoint with muscle content-adjusted dystrophin increasing to 5.46% of normal from a 0.83% baseline at six months ($p < 0.0001$), replicating a 7-fold change from baseline observed in the earlier dose-finding cohort. Unadjusted, mean absolute dystrophin reached 3.71% of normal, which is higher than increases reported for eteplirsen, the current standard-of-care exon-skipping therapeutic indicated for this population (Charleston & coworkers, *Nucleic Acids Research*, 2018), but still low in absolute terms.
 - Improvement relative to pooled placebo was observed across all six prespecified measures at six months, with Time to Rise (TTR) velocity & 10-Meter Walk/Run velocity reaching nominal significance ($p < 0.05$), though the study was not powered for formal hypothesis testing on functional measures. The TTR improvement of 0.04 rise/second exceeded the

published minimal clinically important difference of 0.023 rise/second (Duong & coworkers, *Journal of Neuromuscular Diseases*, 2021). Forced expiration volume (FEV) was preserved at six months compared to a decline in the placebo group. Dyne has initiated the global confirmatory Phase III FORZETTO trial, a 72-week randomized placebo-controlled study of approximately 90 ambulatory participants aged 4 to 18, with change from baseline in rise-from-floor velocity at Week 73 as the primary endpoint, designed to support conversion to traditional approval in the US & regulatory submissions outside the US.

- In regard to one of our coverage stocks that coincidentally is also focused on Duchenne muscular dystrophy therapy development with its small-molecule muscle-regenerating SAT-3247, **Satellos Bioscience (MSLE-Q/MSCL-TSX, Spec Buy, PT US\$16.00)**, the Dyne BLA acceptance reinforces both the opportunity & the strategic rationale for SAT-3247's dystrophin-independent approach to DMD. Let's consider the narrowness of z-rostudirsen's addressable population: exon 51 skipping applies to only approximately 13% of all DMD patients, the largest single exon-skipping target but still a small fraction of the overall disease population (Waldrop & coworkers, *Journal of Neuromuscular Diseases*, 2020; Bladen & coworkers, *Human Mutation*, 2015). Including the four currently approved ASO therapies (exons 51, 53, 45) & Dyne's earlier-stage FORCE programs (exons 53, 45, 44, 55), a meaningful majority of DMD patients remain without a mutation-specific therapeutic option. SAT-3247, which targets AAK1 to enhance endogenous muscle repair & regeneration independent of dystrophin & regardless of exon mutation status, is positioned to address the full DMD genotype spectrum.
- The z-rostudirsen BLA also commercially validates the DMD therapeutic market at a point where Dyne is willing to execute a ~US\$375M financing on a ~US\$3.9B pre-money market capitalization to build a launch infrastructure for an exon 51-specific franchise. The level of capital commitment to a mutation-specific slice of the DMD population certainly validates the commercial potential for a genotype-agnostic therapy with broader addressability. However, the regulatory read-through is limited: z-rostudirsen's accelerated approval pathway relies on dystrophin expression as a surrogate endpoint, a precedent that does not extend to SAT-3247, which produces no dystrophin. SAT-3247's accelerated approval viability, if pursued, would require FDA acceptance of functional endpoints or biomarkers such as MRI-measured muscle fat fraction as surrogate. A post-BASECAMP Type B meeting with FDA would elucidate these details.
- **Royalty Pharma (RPRX-Q, NR) acquires partial royalty rights for clirimitug, a Phase III-stage TTR-fibril-depleting mAb for treating transthyretin amyloid cardiomyopathy (ATTR-CM), currently in Phase III development with AstraZeneca's Alexion rare disease unit.** The swiss-based originator of clirimitug, Neurimmune (private) initially licensed the program to AstraZeneca in 2022 for US\$30M upfront & up to US\$730M in development, regulatory, & commercial milestones, but retained low-to-mid-teen royalties on net sales as the licensor. In the current transaction, Neurimmune is monetizing a slice of that retained royalty stream: Royalty Pharma will pay up to US\$425M (US\$125M upfront, US\$125M in Q1 2027, & up to US\$175M in clinical & regulatory milestones) in exchange for a 3% to 4% royalty on worldwide net sales of clirimitug, carved from Neurimmune's existing entitlement. Neurimmune retains the majority of its royalty & milestone interests. The economic flow, should clirimitug reach market, runs from AstraZeneca (as the commercializing party) to both Neurimmune & Royalty Pharma as concurrent royalty recipients.
- Clirimitug is a recombinant human monoclonal antibody designed to selectively bind misfolded & aggregated forms of transthyretin & trigger the recruitment & activation of phagocytic immune cells to remove existing amyloid deposits (Garcia-Pavia & coworkers, *New England Journal of Medicine*, 2023). Clirimitug is being tested in a medical environment where alternative mechanistically-distinct therapies already exist, including TTR stabilizers like Pfizer's (PFE-NY, NR) tafamidis/Vyndaqel or BridgeBio's (BBIO-Q, NR) acoramidis/Attruby, & TTR gene silencers like Alnylam's (ALNY-Q, NR) own patisiran/Onpattro & vutrisiran/Amvuttra or AstraZeneca's (AZN-LN, NR) eplontersen/Wainua. These therapies certainly slow disease progression by preventing new amyloid accumulation but they do not address the pre-existing cardiac amyloid burden that drives mechanical dysfunction & diastolic heart failure. Long-term follow-up data from the Phase I NI006-101 trial published in *Nature Medicine* showed time- & dose-dependent reductions in cardiac amyloid burden, cardiac biomarkers, & improvements in structural & functional cardiac parameters over a median duration of >29 months (Kahr & coworkers, *Nature Medicine*, 2026). The pivotal Phase III DepleTTR-CM trial evaluating clirimitug's effect on all-cause mortality & recurrent cardiovascular events is actively enrolling patients, with efficacy data expected in F2028.

Exhibit 15. Current Landscape of Therapies for Transthyretin Amyloid Cardiomyopathy



Source: Adapted from *Journal of the American College of Cardiology: Heart Failure* (2025). Vol. 13, pp. 685–694.

- The timing of this deal is notable given the recent clinical failure of Wainua (eplontersen) in the Phase III CARDIO-TTRansform trial, the largest ATTR-CM study conducted to date (1,432-patients), which did not meet its primary composite endpoint of cardiovascular mortality & recurrent cardiovascular events when added to standard care over 140 weeks. The failure appeared largely driven by the futility of adding a TTR gene silencer on top of an existing TTR stabilizer (like cilramitug); a prespecified subgroup of patients receiving eplontersen monotherapy (without baseline stabilizer therapy) showed fewer composite events with nominal significance, although no indication that AstraZeneca has announced plans to pursue regulatory approval on the basis of a subgroup analysis.
- The ATTR therapeutic landscape provides some interesting context for the lipid nanoparticle (LNP) technology class & thus for some interesting context at least for us when we reflect on our legacy coverage universe. Alnylam's Onpatro (patisiran), approved in 2018 as the first-ever RNAi therapeutic, delivers TTR-silencing siRNA using Arbutus Biopharma's (ABUS-Q, NR) proprietary LNP delivery system, which encapsulates the RNA cargo & facilitates hepatocyte uptake (Adams & coworkers, *New England Journal of Medicine*, 2018). Arbutus is a legacy coverage stock of ours, at least when it was branded as Tekmira & when it was exclusively focused on developing LNP-based RNAi therapeutics, with a pipeline that was not limited to Onpatro/patisiran.
- The firm's historic share price trajectory actually rocketed upward in prior years less from Onpatro/patisiran's clinical/commercial success than from the early preclinical success of a Zaire Ebola virus (ZEBOV) RNA polymerase L-protein-targeted formulation called TKM-Ebola (also called TKM-130803) that performed well in a non-human primate study published in May/10 in *The Lancet*. The formulation certainly mitigated Ebola infection in test animals but in human testing it simultaneously triggered an overproduction of pro-inflammatory cytokines that motivated Tekmira to discontinue its development in FQ215. As an aside, the clinical history of this specific LNP-RNAi formulation was summarized in a Feb/20 editorial published in *eBioMedicine*.
- Shifting back to ATTR-CM & Onpatro, Arbutus receives tiered royalties of 1.00% to 2.33% on global Onpatro net sales under a 2012 license agreement. In an adjacent but mechanistically distinct application of LNP technology, Rakovina Therapeutics (RKV-TSXV, NR), which we have discussed in prior weeklies, is collaborating with NanoPalm (Private) on AI-designed patterned LNPs (pLNPs) for small molecule oncology drug delivery. Preclinical formulation data on NanoPalm's EnsaliX-designed pLNP encapsulation of Rakovina's bifunctional PARP/HDAC inhibitor kt-3283 were

presented at AACR 2026, demonstrating uniform particle size, stable colloidal behavior, & structured surface texture predicted to enhance cellular uptake. The NanoPalm/Rakovina application is worth noting as an emerging use case for the LNP chassis beyond gene silencing.

- **Repligen (RGEN-Q, NR) has agreed to acquire BioLife Solutions (BLFS-Q, NR) for approximately US\$1.5B, consolidating the biopreservation media platform involved in commercial cell therapy manufacturing.** BioLife shareholders will receive a combination of cash (36% of deal value) & RGEN shares (64% of deal value), with BioLife's consolidated valuation representing about 11x 2027 consensus revenue estimates. A revenue value that high implies that EBITDA or cash flow (or both) were more germane to Repligen's calculations, but it is not outlandishly high when considering the revenue multiples ascribed to molecular diagnostics or analytical equipment manufacturers that we have analyzed in prior Weeklies & only a slight premium to comparable bioprocessing transactions that we reviewed for this analysis. Repligen expects at least US\$20M in first-year cost synergies & once achieved, adjusted net income accretion is expected to climb by at least US\$0.05/shr in the first-year post-integration, increasing to US\$0.25/shr in subsequent years, excluding any revenue augmentation that the integrated firm could achieve. The transaction is on pace to close by end-of-year F2026.
- The acquisition centers on CryoStor, cryopreservation medium used with 18 commercially approved cell therapies & the majority of U.S. commercially sponsored cell therapy clinical trials. CryoStor's formulation was designed around the phenomenon of cryopreservation-induced delayed-onset cell death (CIDOCD), first characterized by Baust & coworkers in the late 1990s: the freeze-thaw cycle activates apoptotic & necrotic stress pathways that cause substantial cell loss 24 to 72 hours post-thaw, damage that is invisible in immediate viability assessments but critical to therapeutic potency (Baust & coworkers, Cell Transplantation, 2001).
- The CryoStor medium targets these intracellular pathways, incorporating free radical scavengers & optimized ionic buffering. This supports the mitigation of delayed cell death relative to dimethyl sulfoxide (DMSO)-only preparations, which focuses on reducing osmotic shock (H₂O efflux) post freeze. DMSO is a commonly used cell membrane-stabilizing, cryopreserving chemical used ubiquitously in cytology. Once a clinical program validates its manufacturing process with CryoStor through late-stage development & into commercial production, switching is time-consuming & expensive, creating durable competitive positioning & recurring revenue tied to production volumes. Repligen's existing bioprocessing platform (filtration, chromatography, process analytics) complements upstream in a manufacturing workflow; BioLife fills the downstream gap in preservation & cold-chain logistics, with management projecting commercial cell therapy revenues to grow at more than 20% annually through the end of the decade.
- The transaction speaks to a broader recognition that cell-based therapeutic approaches, regardless of modality or disease area, share a common enabling challenge - maintaining cell viability & function during the manufacturing-to-delivery continuum. For the CAR-T & allogeneic cell therapies that anchor BioLife's commercial franchise, a major challenge is cryopreservation during storage & transport. For cell-based approaches outside oncology, the delivery problem takes different forms but is no less critical. ON-based Sernova Biotherapeutics (SVA-TSX, NR), as we have discussed in these pages before, is developing a Cell Pouch bio-hybrid organ for islet cell transplantation in type 1 diabetes, where the enabling challenge is creating a vascularized, immunoprotected environment that supports long-term islet engraftment & function in vivo. Interim Phase I/2 data have shown 8 of 12 patients achieving insulin independence, with islet survival demonstrated out to five years. The underlying scientific problem is analogous: whether cells are being frozen for shipment or transplanted into a subcutaneous pouch, their therapeutic utility depends on infrastructure that preserves viability & enables function at the point of care. Repligen's willingness to pay a premium multiple for what is essentially delivery infrastructure validates the thesis that these enabling platforms are becoming commercially material in their own right as cell-based therapies grow across indications.

Capital Markets Summary

Exhibit 16. EBITDA Or EPS-Positive Canadian Healthcare Stocks

Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 23-Jul	Mkt Cap (M)	Mkt Cap (C\$M)	Ent. Value (M)	Ent. Value (C\$M)	EV/EBITDA			Price/Earnings		
									(T12M)	FY1	FY2	(T12M)	FY1	FY2
Profitable Canadian healthcare firms - specialty services ^{2,4}														
DRI Healthcare Trust	CAD	DHT.UN	55.0	\$17.79	978	978	1,546	1,546	6.7x	6.5x	6.7x	NA	7.5x	7.3x
Jamieson Wellness	CAD	JWEL	41.5	\$41.01	1,701	1,701	2,179	2,179	13.5x	12.2x	10.9x	23.2x	19.1x	16.4x
K-Bro Linen	CAD	KBL	13.0	\$46.32	602	602	887	887	8.0x	8.2x	7.9x	29.2x	22.8x	18.9x
Medical Facilities ¹	CAD	DR	16.2	\$12.73	206	291	325	457	5.4x	5.5x	5.5x	15.0x	6.9x	16.7x
Microbix Biosystems	CAD	MBX	137.2	\$0.31	43	43	41	41	NA	NA	NA	NA	NA	NA
Savaria	CAD	SIS	72.1	\$30.72	2,216	2,216	2,390	2,390	12.6x	11.8x	10.8x	27.8x	22.3x	19.9x
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales ²														
Aurinia Pharma	USD	AUPH	128.6	\$15.33	1,971	2,777	2,335	3,289	11.7x	NA	NA	6.8x	16.1x	12.5x
Bausch Health	USD	BHC	373.5	\$4.56	1,703	2,399	31,245	44,016	6.2x	5.7x	5.9x	NA	1.1x	1.1x
BioSynt	CAD	RX	11.5	\$14.54	167	167	162	162	12.5x	10.1x	8.7x	18.1x	16.3x	13.5x
Cipher Pharma ¹	CAD	CPH	25.4	\$11.64	296	417	408	575	15.2x	13.6x	11.6x	9.6x	12.9x	11.1x
HLS Therapeutics ¹	CAD	HLS	31.3	\$2.99	93	132	176	248	10.7x	9.0x	7.6x	NA	NA	NA
Knight Therapeutics	CAD	GUD	98.2	\$9.68	951	951	877	877	10.0x	11.2x	10.6x	NA	50.9x	44.0x
Medexus Pharma ¹	CAD	MDP	32.0	\$3.63	116	164	186	262	12.1x	11.9x	8.1x	49.0x	NA	12.0x
Profitable Canadian healthcare firms - eldercare services or infrastructure developers														
CareRx	CAD	CRRX	63.5	\$3.35	213	213	276	276	8.9x	7.6x	6.7x	7.8x	27.9x	14.8x
Chartwell Retirement	CAD	CSH.UN	325.2	\$22.30	7,252	7,252	9,952	9,952	23.1x	19.4x	17.6x	NA	NA	54.4x
Extendicare	CAD	EXE	95.0	\$37.33	3,548	3,548	3,552	3,552	18.4x	14.1x	12.4x	27.0x	26.9x	24.6x
Vital Infrastructure	CAD	VITL.UN	250.0	\$5.68	1,420	1,420	2,780	2,780	12.2x	13.4x	13.1x	NA	NA	NA
Nova Leap Health	CAD	NLH	87.3	\$0.37	32	32	34	34	11.6x	NA	NA	NA	NA	NA
Sienna Senior Living	CAD	SIA	110.8	\$22.87	2,533	2,533	3,787	3,787	24.4x	19.0x	16.7x	48.6x	40.1x	35.2x
Profitable Canadian healthcare firms - medical equipment distribution/sales ³														
Covalon Technologies	CAD	COV	27.6	\$2.05	57	57	43	43	46.6x	11.3x	8.9x	34.4x	22.8x	17.1x
Viemed Healthcare	USD	VMD	38.3	\$11.88	455	455	646	910	8.7x	7.0x	6.2x	30.7x	26.1x	19.5x
Profitable Canadian healthcare firms - healthcare IT or digital IT services firms ⁵														
Healwell AI	CAD	AIDX	303.5	\$0.69	209	209	274	274	NA	39.1x	17.1x	NA	NA	NA
Hydreight	CAD	NURS	53.7	\$4.40	236	236	220	220	45.0x	9.7x	6.1x	52.1x	14.7x	8.7x
Kneat.com ⁵	CAD	KSI	96.7	\$6.47	626	881	601	601	NA	35.9x	23.2x	NA	NA	NA
Vitalhub	CAD	VHI	63.4	\$6.67	423	596	304	304	11.4x	8.8x	7.4x	56.3x	30.9x	22.0x
Well Health	CAD	WELL	255.5	\$4.06	1,037	1,037	1,756	1,756	8.1x	9.5x	8.5x	38.5x	16.8x	19.2x
Average									14.9x	13.1x	10.4x	29.7x	21.2x	19.4x
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

² Theratechnologies (TH-T) acquired in Sept/25 by CB Biotechnology/Future Pak for US\$4.20/shr; Andlauer's acquisition by UPS (UPS-NY, NR) closed in Nov/25

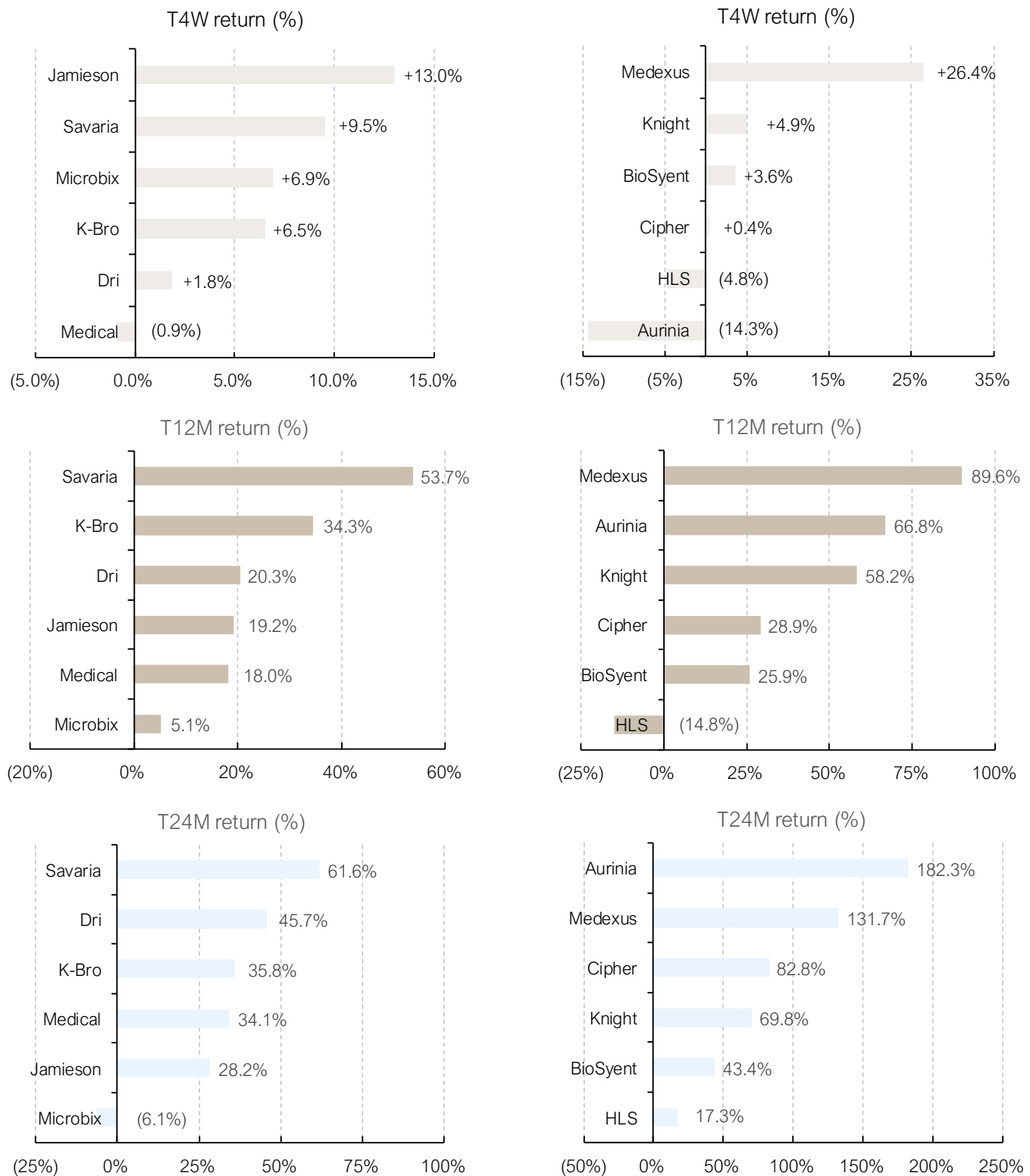
³ Quipt Home Medical was acquired by Kingswood Capital & Forager Capital for US\$3.65/shr in Dec/25, transaction closed in Mar/26

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

⁵ Kneat.com was bid to be acquired in Jun/26 by Thoma Bravo LP for C\$650M; transaction close expected during FQ3/26

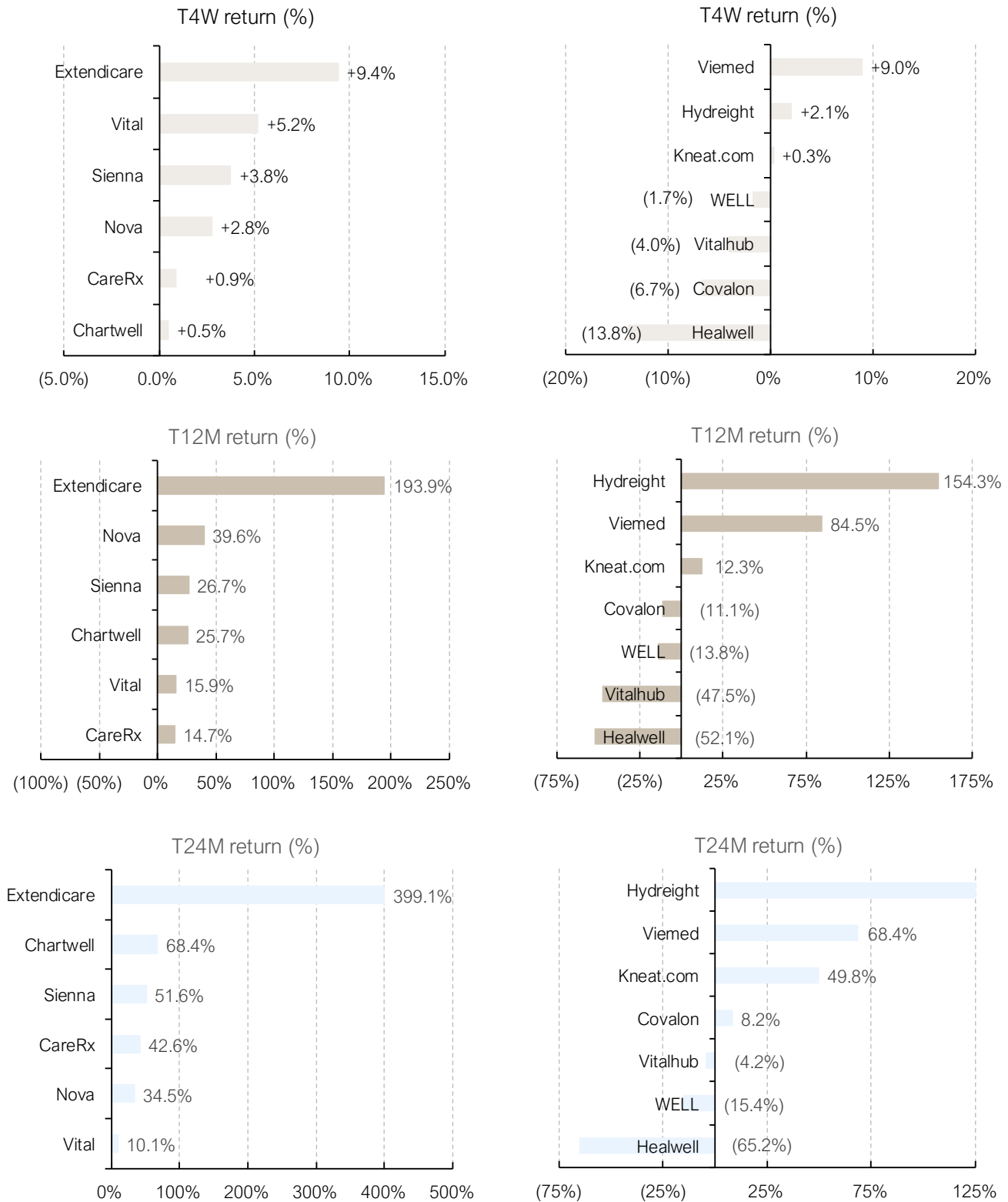
Source: Refinitiv, company reports, Leede Financial

Exhibit 17. 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 18. 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 1,368%*)

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Buy	The security represents attractive relative value and is expected to appreciate significantly from the current price over the next 12-month time horizon.
Speculative Buy	The security is considered a BUY but carries an above-average level of risk.
Hold	The security represents fair value and no material appreciation is expected over the next 12-month time horizon.
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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	5
Extendicare EXE-TSX	None
K-Bro Linen KBL-TSX	None
Medexus Pharmaceuticals MDP-TSX	None
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