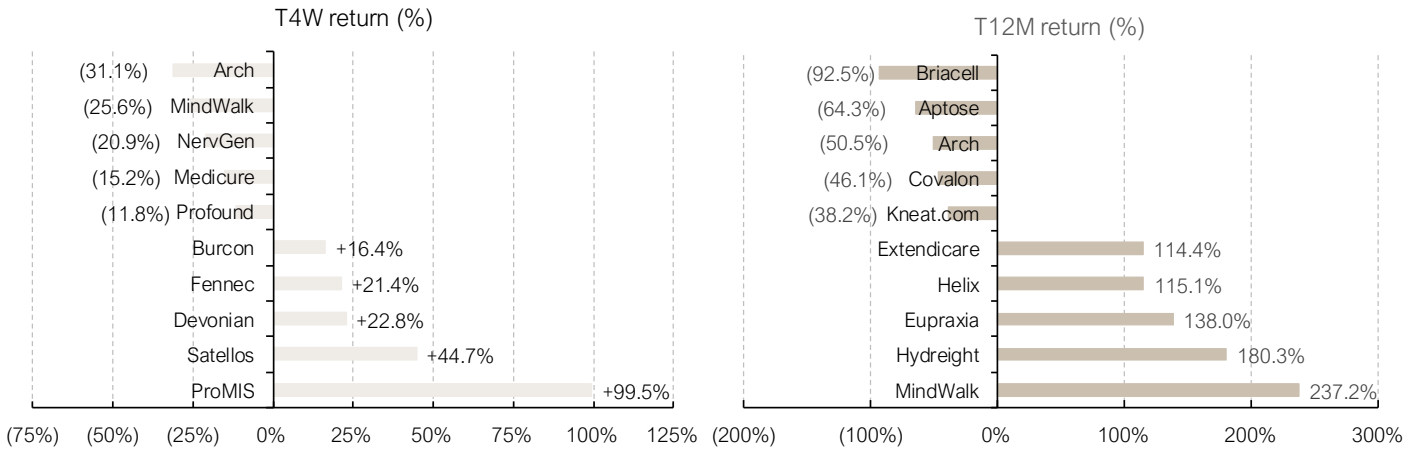
Core Highlights of the Week

Top Movers

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



Source: Leede Financial, Refinitiv

Updates From Our Healthcare Universe

- **Reviewing recent events & clinical priorities for anti-cancer virus developer Oncolytics Biotech.** Earlier this month, CA-based reovirus developer Oncolytics Biotech (ONCY-Q, Spec Buy, PT US$4.00) provided an update on its clinical priorities for its proprietary anti-cancer reovirus formulation pelareorep, indicating that it received Fast Track Status from the US FDA for a clinical program in which Oncolytics (either alone or with partnership participation) drives forward with a colorectal cancer program, the details for which we describe below. Colorectal cancer is a plausible target market for the drug based on Oncolytics' overall clinical history that does include some Phase II programs targeting the indication, though at present, our model overtly ascribes value to advanced pancreatic cancer & to HER2-negative/hormone receptor-positive metastatic breast cancer based on our review of the separate Phase II history is published for pelareorep in both indications.

  - There are a few reasons why colorectal cancer is a justifiable target market for Oncolytics to pursue, independent of the fact that the US FDA clearly agrees through the Fast Track Designation just conferred. The designation is ascribed to a specific colorectal cancer subpopulation – second line patients presenting with metastatic disease that present with defined mutations in the Kras oncogene & who simultaneously present with microsatellite-stable disease - & with pelareorep to be combined with a pre-specified chemotherapy regimen that is frequently used to treat metastatic colorectal cancer, a combination of the VEGF-targeted mAb bevacizumab (Roche/Genentech's [ROG-SW, NR] Avastin), the folic acid derivative leucovorin, the nucleoside analog 5-fluorouracil & the DNA topoisomerase I inhibitor drug irinotecan (collectively abbreviated in the medical literature as FOLFIRI).

  - We stand by our positive view on the medical prospects for pelareorep, usually if not necessarily in combination with some other form of chemotherapy or immune therapy whose own anti-cancer activity is exacerbated by pelareorep administration, but the firm has certainly moved the goal posts a few times in recent years on timelines to pivotal data,

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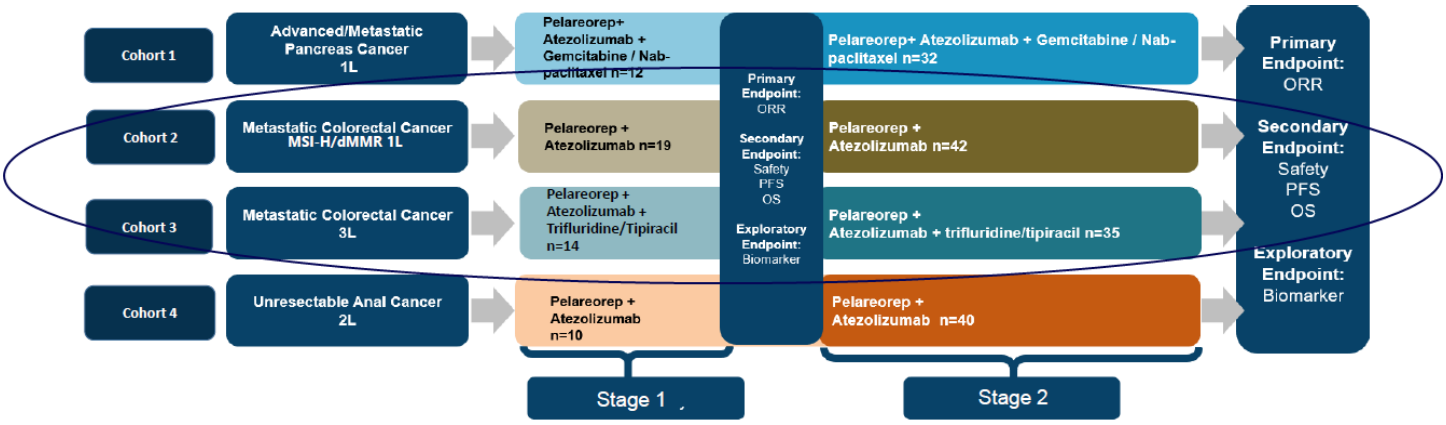
shifting priorities to breast cancer, then to pancreatic cancer & now to colorectal cancer, & eventual clinical performance in ongoing or pending clinical studies could motivate supplemental strategic shifts in coming quarters. Accordingly, it seems likely that our valuation has potential to remain fluid at least in the near-term as we assess future Phase II colorectal cancer data, specifically disease-specific cohort data in the ongoing GOBLET trial for which positive tumor response/survival data could shift priorities again to incorporate squamous cell anal cancer as a secondary indication.

- But to focus on colorectal cancer specifically, it is certainly justified in our view to more comprehensively explore pelareorep's prospects in this indication, for a few reasons. First of all, we have long endorsed any strategy that targets pelareorep toward solid tumor forms that harbor mutations in the Kras gene, since observations that pelareopep exhibited anti-cancer activity toward ras-activated cancers in fact formed the basis for the founding of the company back in 1998 (we have cited the famous *Science* paper documenting this activity as published in Nov/98 by University of Calgary researchers many times in our own ONCY reports). And as far back as 2015 in a review article published by long-time Oncolytics collaborators at Ohio State University in *Annual Reviews of Medicine*, pelareorep (or Reolysin as it was called then) was featured as a novel therapy that even then was thought to have potential in treating colorectal cancer (though without specific regard for the stage of disease or co-administered therapies now thought to be relevant to the Fast Track Designation now conferred).

Exhibit 2. GOBLET Trial – Multiple Gastrointestinal Cancers Being Explored For Susceptibility To Pelareorep, Including Colorectal Cancer Though Not The Form Of Disease (Or The Co-Administered Drugs) To Which Fast Track Status Applies



Source: Adapted from *American Society of Clinical Oncology Gastrointestinal Cancers Symposium (Jan/22)*

- Secondly, colorectal cancer constituted two of the patient cohorts being tested in the ongoing GOBLET trial, though interestingly with neither cohort targeting the disease form to which the new Fast Track Designation applies. But still, some insights into how well pelareorep works to influence survival in colorectal cancer (regardless of biomarker background or stage of disease) should be informative to future colorectal cancer study design.

- Thirdly, Oncolytics does have a published clinical history beyond GOBLET for pelareorep in colorectal cancer, including but not limited to a study published by legacy collaborators at the NY-based Montefiore Medical Center in 2021 in the journal *Clinical Cancer Research*, showing in cellular models of disease that pelareorep exhibited anti-cancer activity in Kras-mutated cell models through a mechanism called autophagy, up-regulating a few of the genes that are relevant to this pathway.

- But more importantly, Oncolytics & its NY-based collaborators published a study in 2020 in the journal *Molecular Cancer Therapeutics* that specifically explored the utility of pelareorep when combined with FOLFIRI & in metastatic oxaliplatin-refractory colorectal cancer patients harboring Kras mutations, exactly relevant to the Fast Track Designation just conferred. In that modestly-sized exploratory trial, three of six patients exhibited partial tumor responses, with median progression-free survival & overall survival of 65.6 weeks & 25.1months, respectively. As a separate observation, the firm showed in this study that activation of tumor-targeted T-cells accompanies pelareorep administration, suggesting though not proving that pelareorep confers anti-tumor activity in Kras-mutated cancer forms at least in part through immune stimulation.

Exhibit 3. Pending Pelareorep Clinical Milestones For Oncolytics

Expected milestone	Clinical trial	Cancer indication	Patient number	Co-administered therapies	Clinical collaborators	Comments
Final biomarker (T-cell clonality, tumor infiltration) data	AWARE-1 (completed)	Metastatic breast cancer (HER2-neg/ HR-pos)	38	Atezolizumab/ Tecen-triq (anti-PD-L1 mAb)	Roche, SOLTI	Q423 (upreg of PD-L1, new T-cell clones)
Interim safety & biomarker data	BRACELET-1 (completed)	Metastatic breast cancer	48	Avelumab/Bavencio (anti-PD-L1 mAb), paclitaxel	Pfizer & Merck KGaA	Q324 (37.5% ORR pela/paclitaxel vs 13.3% paclitaxel)
Interim safety & biomarker (T-cell clonality, tumor infiltration) data	IRENE	Triple-negative breast cancer (HER2-neg/ ER-neg, PR-neg)	25	Retifanlimab (anti-PD1 mAb)	Rutgers Univ, Incyte	H126 (two-year PFS/OS data)
Interim biomarker data (T-cell clonality & CEA-CAM6 expression)	GOBLET	Advanced pancreatic, colorectal, anal cancer	55	Atezolizumab/ Tecentriq (anti-PD-L1 mAb), mFOLFIRINOX	Roche, AIO Studien gGmbH	H126 (safety data for pelareorep-mFOLFIR-INOX, 62% ORR, favorable 2-yr survival)
Objective response rate, survival	GOBLET	Squamous cell anal carcinoma	up to 28	Atezolizumab/ Tecentriq (anti-PD-L1 mAb), mFOLFIRINOX	Roche, AIO Studien gGmbH	33.3% ORR reported at 2025 ASCO meeting; update in H126
Probably response rate & survival	TBD	Second-line oxaliplatin-refractory Kras-mutated MSS colorectal cancer	TBD	FOLFIRI (leucovorin, 5-FU, irinotecan) & bevacizumab	TBD	Expect trial activation by end-of-Q126
Interim response rate, survival	AMBUSH	Refractory multiple myeloma	42	Bortezomib/Velcade or Pembrolizumab/ Keytruda, dexameth	USC, US NCI (started in Oct/22)	H226 (final 3-yr ORR, PFS, OS data)
Commence patient enrollment	Pivotal Phase III	Metastatic pancreatic cancer (first-line)	TBD	Gemcitabine, nab-paclitaxel (Abraxane), anti-PD1 mAb or anti-PD-L1 mAb	Unpartnered as yet	H126 (OS as primary endpoint), data by 2029/30
Commence patient enrollment	Pivotal Phase III	Metastatic breast cancer (HER2-neg/ HR-pos), probably Enhertu (trastuzu-	180	Paclitaxel	Unpartnered	H226 (PFS/OS data possibly by 2030/31)

Source: Adapted from Oncolytics Biotech investor presentations; Leede Financial

- Going back even further to 2018, when Oncolytics published data in collaboration with the Canadian National Cancer Institute from a 103-patient Phase II colorectal cancer trial in the journal *Clinical Colorectal Cancer*, data showed from that trial that combining pelareorep with a similar but distinct chemotherapy regimen to FOLFIRI (a combination that includes oxaliplatin instead of irinotecan but all other drugs are the same, including bevacizumab/Avastin), an increased overall response rate in comparison to control patients (the same drugs but without pelareorep) was observed, but of shorter duration (5 months vs 9 months) & there was no survival benefit either (19.2 months vs 20.1 months). We commented at the time of our original review of these data that colorectal cancer seemed unattractive as a target indication for Oncolytics to pursue but a few features in the Fast Track Designation trial make renewed interest in second-line oxaliplatin-resistant metastatic disease more strategically sound.

- First of all, patients will be second line & thus already refractory to oxaliplatin, one of the co-administered drugs in the 2018 trial. Secondly, patients will receive irinotecan (a drug that like platinum-containing drugs in general disrupts DNA replication, though by a distinct mechanism) as part of the drug cocktail administered along with pelareorep in the new trial. Thirdly, patients in the Fast Track trial will be pre-screened for Kras mutation status & microsatellite instability, neither of which were patient screening criteria in the 2018 study described above. Accordingly, the new Phase II clinical plain in colorectal cancer seems to be sufficiently well-reasoned so as to leverage pelareorep's mode of action. In coming months, we will be closely monitoring timelines to updating Phase II data from the GOBLET trial, as well as closely monitoring timelines to commencing the new Fast Tracked Phase II colorectal cancer trial recently described & simultaneously tracking partnership activity in the pancreatic cancer therapy development realm, with our model still assuming that pancreatic cancer could be Oncolytics' lead indication.

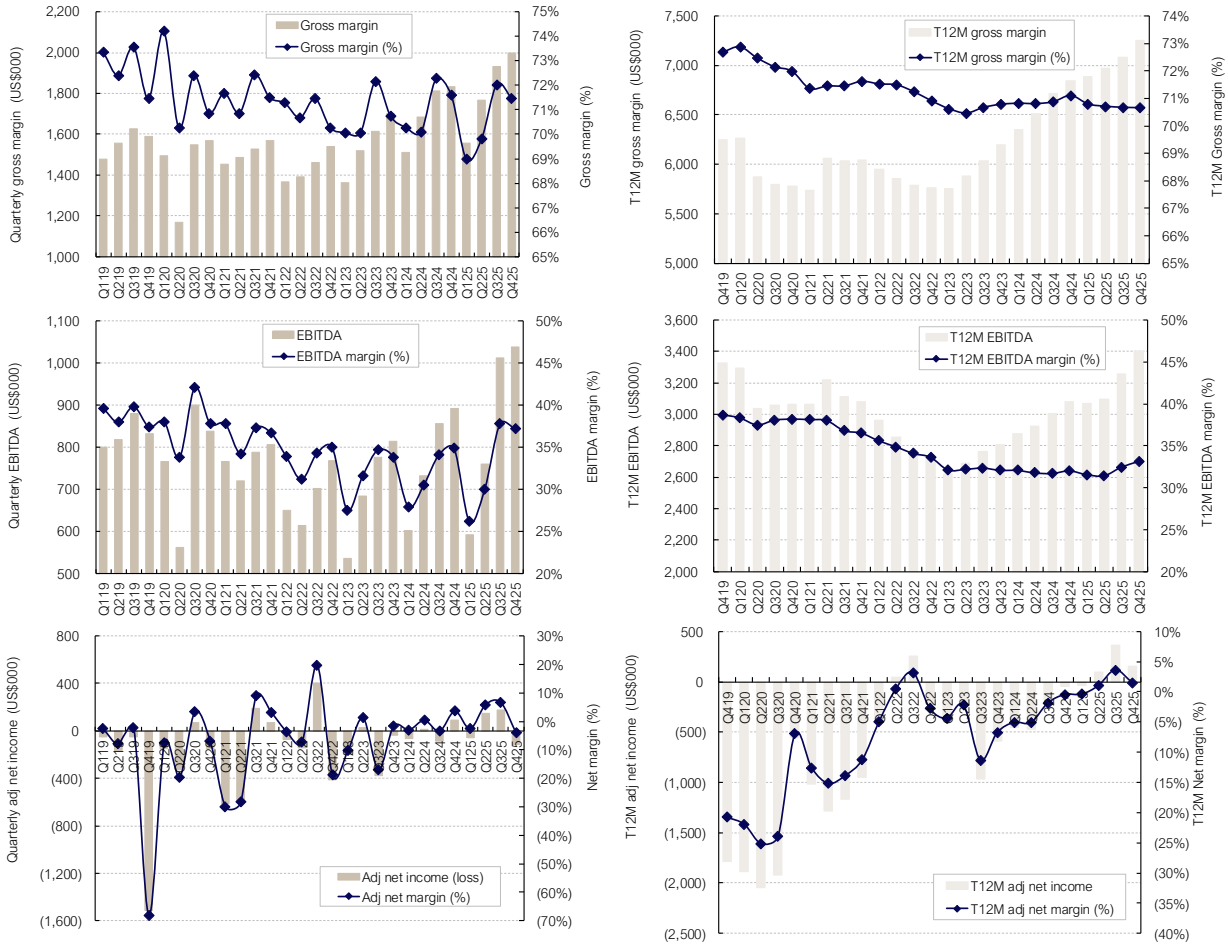
Other Significant Clinical Trial Updates With Relevance To Our Coverage Universe

- **Bausch Health reports FQ425 financial data.** QC-based diversified specialty pharmaceutical firm Bausch Health (BHC-NY, NR), the continuing publicly-traded firm that was spun-out from parent firm Bausch & Lomb in 2018 (a transaction that was preceded by the Biovail-Valeant Pharmaceuticals merger in 2010 & from the Valeant-Bausch & Lomb merger in 2013),

reported quarterly & year-end financial data for the December-end periods; we will focus on FQ425 data & on how it compares with prior quarters rather than on annual data in our commentary below.

- As we show graphically in Exhibits 4 & 5, Bausch reported FQ425 revenue/gross margin/EBITDA of US$2.8B/US$2.0B/US$1.0B, comparing favorably to FQ325 data of US$2.7B/US$1.9B/US$1.0B & y/y to US$2.6B/US$1.8B/US$0.9B, with all three quarters clearly similar on all metrics including margins though with an upward steady trend throughout the three periods. EBITDA margin & relative gross margin were virtually identical in the respective periods at 71.5%/37.2% in FQ425, 72.0%/37.8% in FQ325 & 71.6%/34.9% in FQ424.

Exhibit 4. Quarterly & T12M EBITDA-Net Income Financial Data For Bausch Health, FQ119-to-FQ425



Source: Bausch Health financial filings, Leede Financial

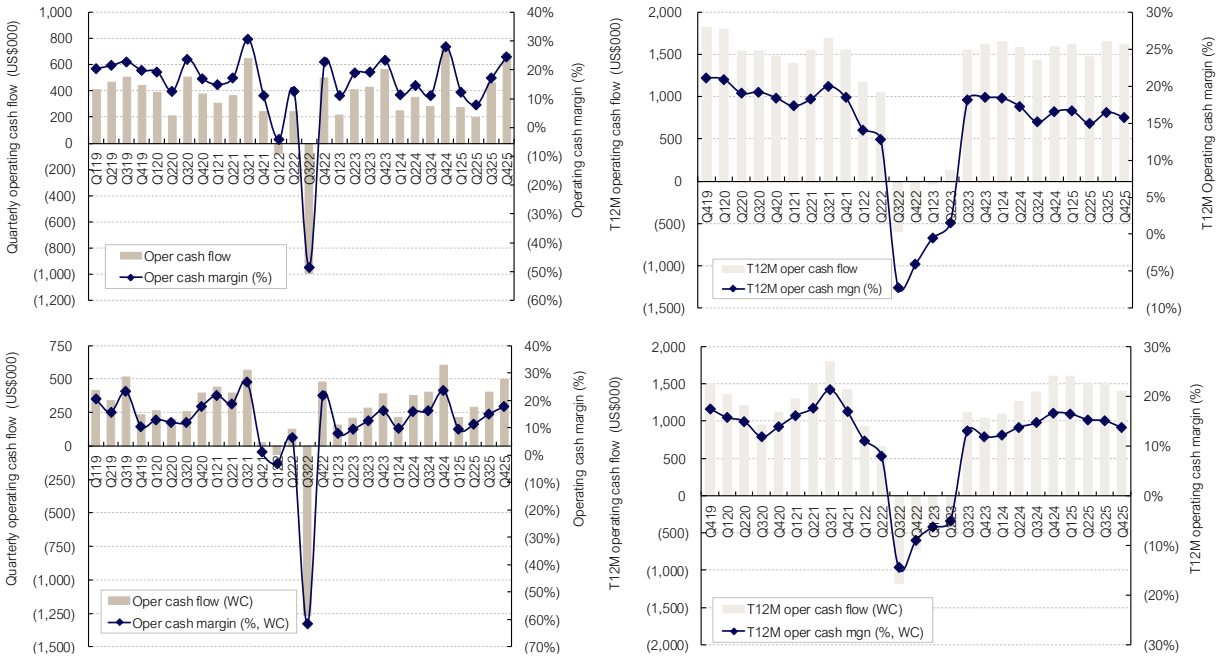
- EBITDA-to-interest coverage ratio in FQ425 was 2.6x, essentially at FQ325 level of 2.5x & identical to FQ424 ratio also of 2.6x; FQ425 debt-to-FQ425 EBITDA run-rate ratio was 5.0x, incrementally below 5.2x recorded in FQ325 but further below FQ424 ratio of 6.1x. We have no major criticism of Bausch's gross margin/EBITDA margin thresholds in comparison to its peers, but its financial risk as conferred by the aforementioned financial ratios, & probably lingering business risk inherent in probable genericization of a major Rx therapy (the irritable bowel syndrome drug sold by division Salix rifaximin/Xifaxan) is contributing to the multiple softness ascribed to Bausch's consensus F2026/27 EBITDA forecasts (6.1x/6.4x). Bausch guided capital markets to expect F2026 revenue of US$10.6B-to-US$10.9B (we assume that stable Xifaxan branded sales are assumed in that guidance) & if achieved would sustain annual revenue growth from F2022 trough level of US$8.1B that grew to US$8.8B in F2023, to US$9.6B in F2024 & to US$10.2B last year.

- While on the topic of Xifaxan, which contributed 85% of Salix's FQ425 revenue of US$693M (so about US$590M), Bausch devotes considerable commentary on its ongoing Paragraph IV litigation with multiple generic drug developers

(Norwich Pharmaceuticals [private] & Amneal Pharmaceuticals [AMRX-Q, NR], specifically), for which supplemental court proceedings are expected to transpire later this year. Proceedings like this usually lead to onset of generic competition, a reality that Bausch itself has exploited during its public markets history, & we assume that Bausch followers have made personal estimates for when a generic Xifaxan could be launched.

- ANDA filings from both Norwich & Amneal are already FDA-approved, indicating that manufacturing capabilities are already in place for both firms. But with Bausch's Salix division generating FQ425 operating income of US$529M (76.3% margin) on total revenue of US$693M, every quarter for which Bausch generates Xifaxan-specific operating income (that in FQ425 alone was likely in the range of US$445M-to-US$455M) is a quarter for which Bausch is motivated to sustain brand preservation through all legal protocols available to it.

Exhibit 5. Quarterly & T12M Cash Flow Data For Bausch Health, FQ119-to-FQ425



** Excluding $1.2B accrued legal settlement payment in FQ322, operating cash flow would have been US$0.22M (or [US$0.05M] after adjusting for working capital*

Source: Bausch Health financial filings, Leede Financial

- We mention Salix (a legacy acquisition for the firm & fun fact, a legacy comparable for a former coverage stock of ours, QC-based GI-focused Axcan Pharma [taken private by TPG Capital back in Q108]) for its focus on genericization-imminent Xifaxan but also for its superior operating margin within the suite of Rx divisions that Bausch operates, with its Diversified Products division also performing well on operating margin at 70.2% in the quarter, with another former acquisition Solta Medical generating 40.1% operating margin in the quarter (actually the lowest margin for Solta since FQ323) & with International & other revenue contributing operating margin in the 26.5%-to-28.2% range.

- FQ425 pure operating cash flow was US$687M or US$1.85/shr, well above FQ325 level of US$458M (US$1.24/shr) but a bit below FQ424 level of US$717M (US$1.95/shr). The firm has no track record of sustaining working capital imbalances in either direction & so we tend not to focus on working capital-adjusted operating cash flow too excessively, but for the record, a sizable tax receivable in the quarter largely contributed to a working capital deficit in FQ425 of (US$192M) that brought consolidated operating cash flow in the quarter to US$495M, up from US$405M in FQ325 but below US$601M in FQ424.

Exhibit 6. Comparable Specialty Pharmaceutical Firms For Bausch Health

Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 19-Feb	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 specialty pharmaceutical firms														
Aurinia Pharmaceuticals	USD	AUPH	131.8	$14.31	1,887	1,887	2,201	2,201	14.9x	10.0x	8.3x	24.8x	15.3x	13.4x
BioSyent	CAD	RX	11.5	$14.80	170	170	147	147	10.3x	11.7x	10.4x	19.4x	17.0x	15.6x
Cipher Pharmaceuticals [1]	CAD	CPH	25.3	$10.72	271	271	380	380	13.8x	10.9x	8.5x	15.8x	18.0x	13.4x
HLS Therapeutics	CAD	HLS	31.3	$4.50	141	141	201	201	9.0x	6.5x	5.6x	NA	NA	NA
Knight Therapeutics	CAD	GUD	98.7	$6.55	647	647	635	635	12.3x	9.7x	10.0x	NA	NA	46.8x
Medexus Pharmaceuticals	CAD	MDP	32.3	$2.85	92	92	107	107	5.7x	4.9x	3.6x	NA	NA	8.9x
Average									**12.9x**	**10.4x**	**9.4x**	**24.6x**	**19.9x**	**18.1x**
Profitable global specialty pharmaceutical firms														
AbbVie	USD	ABBV	1767.4	$228.72	404,236	553,622	640,037	876,563	NA	13.6x	12.4x	NA	15.7x	14.3x
Almirall SA	EUR	ALM	214.8	€ 13.82	€ 2,968	4,790	€ 4,726	7,626	NA	10.4x	8.9x	NA	27.2x	20.3x
Amgen	EUR	AMGN	214.8	$13.82	2,968	4,065	4,726	6,472	NA	10.4x	8.9x	NA	27.2x	20.3x
Biogen	USD	BIIB	146.8	$194.13	28,490	39,019	42,402	58,071	8.7x	9.6x	9.9x	22.0x	12.3x	11.9x
Fresenius	EUR	FREG	563.2	€51.82	29,187	47,096	63,308	102,153	17.1x	15.7x	14.7x	20.9x	14.0x	12.6x
Cardinal Health	USD	CAH	235.3	$224.99	52,944	72,509	81,318	111,369	21.1x	20.5x	18.7x	32.2x	21.9x	19.5x
Dr. Reddy Labs	INR	500124	832.6	Rp1,280	1,065,495	16,062	15,928	240	0.2x	0.2x	0.2x	19.1x	20.7x	23.1x
Gilead Sciences	USD	GILD	1240.7	$152.74	189,501	259,532	279,040	382,160	19.3x	17.6x	16.3x	22.3x	17.5x	15.8x
Incyte Pharmaceuticals	USD	INCY	199.0	$102.99	20,497	28,071	23,214	31,793	16.1x	12.2x	9.5x	15.6x	13.7x	11.7x
Jazz Pharmaceuticals	USD	JAZZ	60.8	$168.72	10,252	14,041	18,581	25,447	16.0x	10.0x	9.0x	NA	7.5x	6.7x
Perrigo	USD	PRGO	137.6	$14.58	2,007	2,748	7,148	9,789	9.7x	10.2x	9.7x	NA	5.5x	5.3x
Puma Biotechnology	USD	PBYI	50.4	$6.68	337	461	378	518	8.3x	NA	NA	8.9x	16.7x	12.6x
Sun Pharma/Ranbaxy	INR	524715	2399.3	Rp1,713	4,110,541	61,966	58,419	881	0.4x	0.3x	0.3x	39.2x	34.3x	30.6x
Teva Pharmaceuticals	USD	TEVA	1164.6	$34.11	39,726	54,407	72,949	99,908	14.1x	14.3x	13.3x	27.7x	12.7x	11.0x
United Therapeutics	USD	UTHR	43.1	$476.05	20,497	28,072	24,281	33,253	14.9x	14.2x	13.2x	16.7x	16.5x	15.3x
Vertex Pharmaceuticals	USD	VRTX	254.0	$470.31	119,475	163,627	154,725	211,903	31.5x	26.7x	22.9x	30.4x	24.4x	21.4x
Viatris	USD	VTRS	1151.8	$16.05	18,486	25,317	43,602	59,716	10.5x	10.4x	9.7x	NA	6.4x	5.8x
Average									**13.4x**	**12.3x**	**11.1x**	**23.2x**	**17.3x**	**15.2x**
Bausch Health	**USD**	**BHC**	**370.9**	**$6.19**	**2,296**	**2,296**	**31,457**	**31,457**	**6.9x**	**6.1x**	**6.4x**	**6.3x**	**1.5x**	**1.6x**

[1] *Share price converted to USD for stocks reporting financial data in USD but for which share value is reported in CAD*

Source: Refinitiv

- **Alzheimer's disease competitive landscape – reflections on clinical drug development programs funded by peers.** Many times during our coverage history of MA-based ProMIS Neurosciences (PMN-Q, Spec Buy, PT US$49.50) we have commented on competitive landscape in the firm's targeted disease indications, including but not limited to Alzheimer's disease for which the firm's beta-amyloid oligomer-targeted mAb PMN310 is undergoing Phase II testing in the 144-patient PRECISE-AD trial (interim six-month cognition/biomarker data expected by us in, coincidentally, six months; one-year cognition/biomarker data thus expected by end-of-F2026 or perhaps in FQ127). We summarized that trial & those milestone timelines in a few PMN updates already this year & will not dwell on them here.

  - The Alzheimer's disease competitive landscape overview that follows was actually inspired by a recent review article published in the American Chemical Society periodical Chemical & Engineering News, in which author Laurel Oldach chose to describe various clinical-stage drugs that unlike PMN310 do not target beta-amyloid antigens (as do the most-recently & successfully FDA-approved mAb drugs targeting Alzheimer's disease like Eisai's lecanemab/Leqembi & Eli Lilly's donanemab/Kisunla by the way, just with distinctive pharmacology to that being employed by ProMIS).

  - The Alzheimer's disease pharmacopeia certainly has room for multiple therapies & possibly even multiple modes of action, & so the article to which we refer was useful to us to reflect on all of the different cognition-relevant pathways that are being exploited by ProMIS' peers in ongoing clinical studies. The article tabulated various drugs & programs, but for our own purposes we supplemented our own tables to include clinical trial details & timelines to data that we will be tracking going forward. Most of the competitive advanced clinical programs were focused on targeting a distinct neural protein called tau which we are quite familiar with not just for its prospect as a target for cognition-relevant drugs but also as a marker for cognitive impairment in both plasma & cerebrospinal fluid. But other biological targets & pathways are being explored, as we summarize in Exhibits 7-to-9.

Exhibit 7. Clinical Studies Focused On Alzheimer's Disease – Monoclonal Antibody Or Vaccine-Based Formulations

Therapy	Molecular target & pharmacology	Lead investigator or institution	Number of patients	Stage of Development	Primary Endpoint	Timeline to Data
mAb- or vaccine-based clinical-stage Alzheimer's disease therapies						
Remternetug (LY3372993)	Pyroglutamated beta-amyloid	Eli Lilly (LLY-NY)	1,667	Phase III (TRAILRUNNER-ALZ1)	Changes from baseline in amyloid plaque levels on PET at one-year	Mar-26
ACI-24.060 (ACI-24)	Beta-amyloid (palmitoyl-ated N-term beta-amyloid-15 peptides, embedded into liposome carrier)	AC Immune, Takeda as commercial partner (4502-JP; ACIU-Q)	176	Phase I/II (ABATE trial)	Multiple endpoints based on cognition or plasma biomarkers at 74 wks; generates polyclonal Ab response to oligomeric & pyroglutamate beta-amyloid forms	Jun-26
BMS-986446	Microtubule binding region tau (MBRT)	Bristol-Myers Squibb (BMY-NY)	310	Phase II/III (TargetTau-1)	Change from baseline in Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB) at 76 weeks	Mar-27
VY7523	Tau (C-terminal epitope)	Voyager Thera-peutics (VYGR-Q)	52	Phase I/II (VY7523-102)	Impact on tau PET at 6-12 mo period; PK in plasma or CCF over same period	May-27
Etalanetug (E2814)	Microtubule binding region tau (MBRT)	Eisai (4523-JP)	197	Phase II (DIAN-TU)	Changes in tau PET during 6-24 mo period; change from baseline in CDR-SB at up to 48 mo; already shown to reduce levels of eMTBR-tau243 in CSF & plasma	Jul-28
MK-2214	Tau (phosphorylated at Ser-413 in C-terminus)	Merck (MRK-NY)	340	Phase II (MK-2214-004)	Change from baseline in CDR-SB or ADAS-Cog13 at 23 mo; changes in tau PET at same time point	Apr-29
ACU193 (sabirnetug)	Beta-amyloid oligomers	Acumen Pharma-ceuticals (ABOS-Q)	542	Phase II (ALTITUDE-AD)	Change from baseline in Alzheimer's Disease Rating Scale Score at 80 weeks	Oct-26
PMN310	Beta-amyloid oligomers (cyclic peptide as Ag mimic)	ProMIS Neuro-sciences (PMN-Q)	144	Phase II (PRECISE-AD)	Change from baseline in CDR-SB or ADCS-ADL at 12 mo; change from baseline in plasma levels of phosphorylated tau at 12 mo	Dec-26

Source: Adapted from *Chemical & Engineering News (Feb/26),* company reports, Leede Financial

- One important point from our clinical trials summary, specifically in Exhibit 7, is that the Chem Eng News article we are citing here did not in fact feature PMN310, or its mechanistic peer drug ACU193 (we added those programs to the exhibit at our own discretion), thus further indicating to us just how under-appreciated or misunderstood is the relevance of beta-amyloid oligomers as a contributing factor to Alzheimer's disease onset & progression.

Exhibit 8. Clinical Studies Focused On Alzheimer's Disease – RNA- Or Gene-Editing-Based Formulations

Therapy	Molecular target & pharmacology	Lead investigator or institution	Number of patients	Stage of Development	Primary Endpoint	Timeline to Data
Nucleic acid-based (antisense/RNAi/gene therapy) clinical-stage Alzheimer's disease therapies						
LY3954068	Tau (antisense RNA; targets *MAPT* gene)	Eli Lilly (LLY-NY)	48	Phase I	Impact on tau in CSF at up to 52 wks	Feb-27
DNL628	Tau (antisense RNA; targets *MAPT* gene)	Denali Therapeutics (DNLI-Q)	68	Phase Ib	Uses transferrin receptor targeting to cross BBB (TransportVehicle); PK profile, impact on pTau181 in CSF at 25 wks	Feb-27
NIO752	Tau (antisense RNA; targets *MAPT* gene)	Novartis (NVS-NY)	36	Phase I	Tau levels in CSF at 85 days; lead indication is progressive supranuclear palsy (accumulation of four-repeat tau isoforms)	Jan-28
BIIB080 (ISIS 814907)	Tau (antisense RNA; targets *MAPT* gene)	Biogen-Ionis (BIIB-Q, IONS-Q)	416	Phase II	Change from baseline in CDR-SB, ADAS-Cog 13 or ADCS-ADL at 76 wks	Jan-28
LX1001	ApoE4 (AAVrh10-based; encodes ApoE2 gene)	Lexeo Therapeutics (LXEO-Q)	10	Phase I	Increased ApoE2 expression ApoE4 homozy-gotes (15x more likely to develop AD) in legacy 15-pt Ph II trial in Nov/24	Nov-28
ALN-5288	Tau (siRNA; targeting MAPT gene)	Alnylam Pharma-ceuticals (ALNY-Q)	50	Phase I	Change in total tau in CSF at 32 mo; PK profile (binds to tau mRNA, triggers degradation)	Mar-30

Source: Adapted from *Chemical & Engineering News (Feb/26),* company reports, Leede Financial

- This is not the only example of oligomer omission we have seen in review articles on the Alzheimer's disease pharmacology landscape. We believe that the medical literature in support of our PMN investment thesis (& the PMN310 royalty revenue projections on which our PMN valuation is based) is strong & thus worth at least some emphasis in the medical literature. We of course emphasize the medical relevance of amyloid oligomers in our PMN coverage.
- As shown in the relevant exhibits, there are a few sizable advanced clinical programs that are of particular interest to us, not because they are relevant to PMN310 mechanism of action (& thus on oligomer pathophysiology) but because of their scale & advanced stage of development – Eli Lilly's [LLY-NY, NR] TRAILRUNNER-ALZ1/remternetub trial, Bristol Myers Squibb's [BMY-NY, NR] ATargetTau-1/BMS-986446 trial, Biogen's [BIIB-Q, NR] BIIB080 trial & AriBio's [private] Polaris-AD/AR1001 trial are four of many that we will closely monitor in coming quarters.

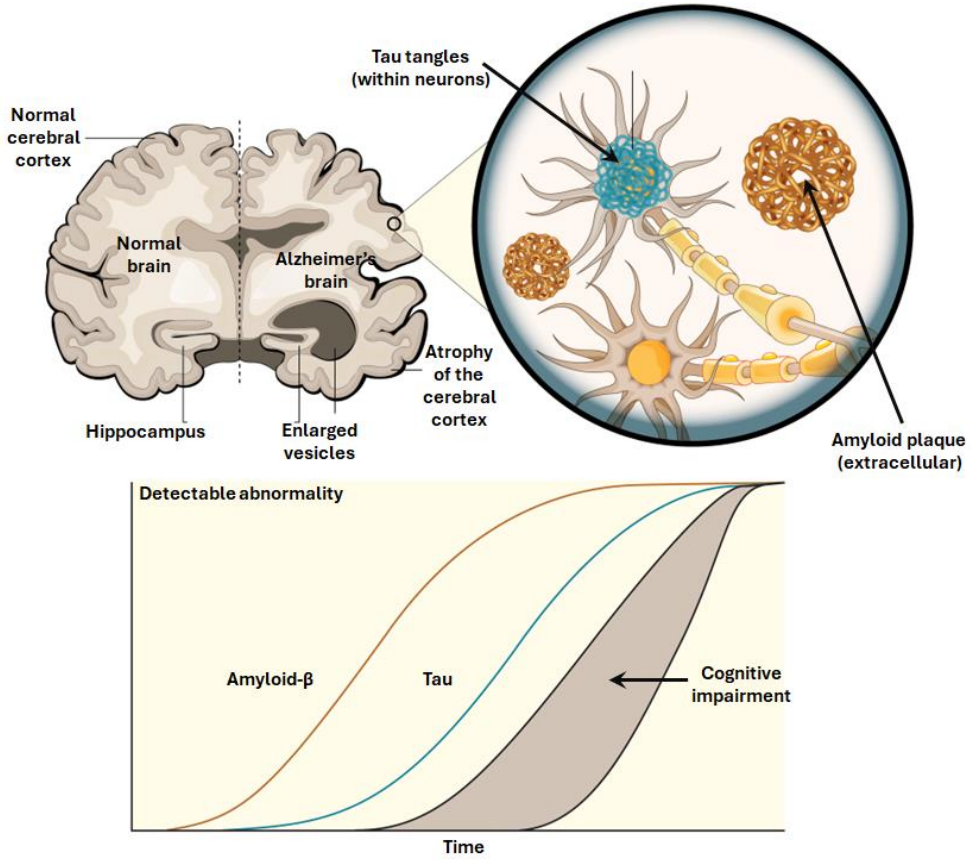
Exhibit 9. Clinical Studies Focused On Alzheimer's Disease – Small Molecule-Based Formulations

Therapy	*Molecular target & pharmacology*	*Lead investigator or institution*	*Number of patients*	*Stage of Development*	*Primary Endpoint*	*Timeline to Data*
Small-molecule-based clinical-stage Alzheimer's disease therapies						
Hydroxypropyl-beta-cyclodextrin (Trappsol Cyclo)	ApoE (thought to improve nerve myelination via cholesterol transport)	Cyclo Therapeutics (Rafael Holdings; RFL-NY)	90	Phase II (EAD501)	Change from baseline in CDR-SB or ADAS-Cog13 at 6 mo; firm mostly focused on Ph III Niemann-Pick Disease Type C1 program	Mar-24
CS6253 (Cogpep)	ApoE (ABCA1; ATP-dependent cholesterol efflux pump agonist)	Artery Therapeutics (private)	66	Phase I (ApoE4 carriers only)	PK characterization; promoted nerve myelination in preclinical testing in ApoE4 expressers (*Alzheimer's & Dementia; Jan/25*)	Jul-24
VNA-318	Metabolism (impacts mitophagy-mitochondria turnover)	Vandria SA (private)	92	Phase I	Single- & multiple-ascending dose safety/PK testing at one week	Nov-25
MNA-001 (MTX46943)	Inflammation (TREM2 agonist)	Muna Therapeutics ApS (private)	NA	Phase I	TREM2 (triggering receptor expressed on myeloid cells 2; regulates microglial cells that phagocytose misfolded proteins like beta-amyloid); PK data; partnered with GSK	Sep-26
Bumetanide (Bumex; loop diuretic)	ApoE (proposed to flip ApoE transcriptome in animal models)	Stanford University (private)	40	Phase I (BumxAD)	Change from baseline in CDR-SB or ADAS-Cog13 at 6 mo	Dec-26
Metformin	Metabolism (biguanide, reduces liver glucose production)	Columbia University (private)	326	Phase II/III (MAD trial)	Change from baseline in PACC-ADCS cognition scale at 18 mo; ApoE4 genotype impact	Apr-27
AR1001	Inflammation (pyrrole-pyrimidinone phospho-diesterase 5 inhibitor)	AriBio (private)	1,535	Phase III (Polaris-AD)	Change from baseline in CDR-SB or ADAS-Cog13 at 12 mo; CSF biomarkers at 36 mo (210-pt Ph II showed impact on plasma biomarkers, not cognition; *J Prev Alz Dis 2025*)	Dec-27
Buntanetap (posiphen, ANVS-401)	Beta-amyloid (physostigmine analog, inhibits translation of neurotoxic proteins)	Annovis Bio (ANVS-Q)	760	Phase III	Change from baseline in ADCS-iADL or ADAS-Cog13 cognition scales at 18 mo; regulates mRNA translation of beta-amyloid precursor protein, alpha-synuclein, TDP-43	Jun-28

Source: Adapted from *Chemical & Engineering News (Feb/26),* company reports, Leede Financial

- But the other news-du-jour this week was from a firm that we actually cite in Exhibit 7 in Swiss drug developer AC Immune SA (ACIU-Q, NR), which just halted enrollment in a different Alzheimer's disease-focused beta-amyloid-based vaccine formulation called ACI-35.030, or JNJ-2056 in partner Johnson & Johnson's [JNJ-NY, NR] pipeline. Details described in a securities regulatory document vaguely indicated that aspects of the trial are being evaluated, which could mean just about anything related to manufacturing or sluggish patient enrollment or lack of cognitive impact at interim analysis or some combination of all three. Independent of this, AC Immune appears to be soldiering ahead with ACI-24.060, the beta-amyloid-based vaccine formulation that we do incorporate into Exhibit 7, for which biomarker & cognition-based endpoints are expected to be assessed later this year.
- But in conclusion, we do not believe that any beta-amyloid-targeted mAbs or beta-amyloid-based vaccine formulations that do not specifically exploit the unique neurotoxicity that oligomers are known to confer have any direct impact on PMN310 clinical risk & we are maintaining our rating/PT on PMN as a consequence. Though ProMIS has other mAbs in its pipeline that target other disease-relevant misfolded proteins (misfolded TDP-43 in amyotrophic lateral sclerosis with PMN442 & misfolded alpha-synuclein in Parkinson's disease with PMN267, for which we believe IND-enabling preclinical pharmacology testing is ongoing), our attention & our valuation is squarely focused on PRECISE-AD & on the interim efficacy milestones on the horizon later this year.

Exhibit 10. Proposed Pathways For Alzheimer's Disease Pathophysiology, Based On Imaging Data Correlating Detection Of Specific Biomarkers With Timelines To Cognitive Impairment

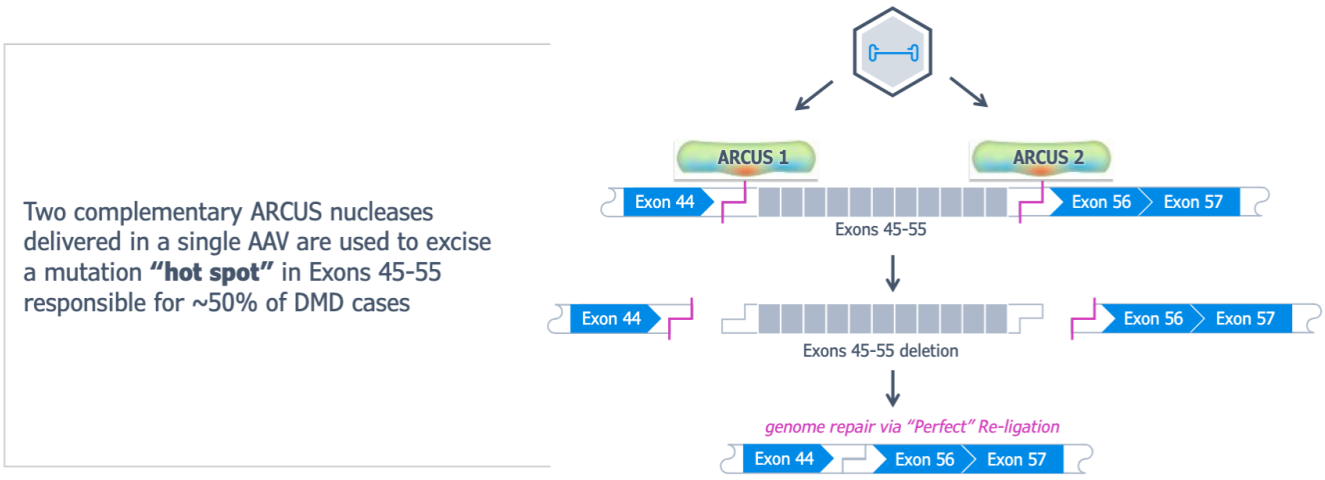


Source: Adapted from *Chemical & Engineering News (Feb/26)*

- **Several DMD-specific stories within the landscape for recently-initiated Satellos Biosciences (MSLE-Q, PT: US$16.00).** Of note, Satellos dosed the first participant in BASECAMP, its Phase 2 pediatric DMD study, on February 12, 2026. BASECAMP is a three-month, randomized, double-blind, placebo-controlled, proof-of-concept study designed as a potential pivotal trial, which would allow positive results to support a regulatory filing without requiring a separate confirmatory study. The study will enroll 51 ambulatory boys with DMD aged 7–9 years across up to 25 clinical sites spanning the United States, Europe, the United Kingdom, Australia, Canada, and Serbia. Primary endpoints include safety, tolerability, and effect on muscle force (measured by dynamometry), with secondary endpoints assessing muscle quality, function, and regeneration. As we have previously covered, Satellos closed a US$57.2M public offering on February 9, establishing pro forma cash of approximately US$88M; a runway sufficient to fund both BASECAMP and LT-001 (the Phase 1/2 trial) through key data readouts. Given the three-month study duration, we anticipate data by Q3/26, with full data expected by end of F2026.

    - **Precision BioSciences (DTIL-Q, NR) received FDA clearance to initiate a Phase 1/2 gene editing trial (FUNCTION-DMD) for DMD.** Their candidate, PBGENE-DMD, uses the same AAV delivery vehicle as microdystrophin therapies like Elevidys, but with a fundamentally different payload. Rather than introducing a synthetic micro-transgene, the AAV encodes two ARCUS nucleases that make permanent cuts in the patient's own chromosomal DNA, excising the exon 45–55 hotspot and enabling expression of near-full-length dystrophin (versus ~33% for microdystrophins). The therapeutic goal is conceptually similar to PMO exon-skipping therapies (Exondys-51, Amondys-45) in that both restore the dystrophin reading frame by removing the same mutational hotspot, but PBGENE-DMD acts permanently at the DNA level rather than transiently at the RNA level, eliminating the need for chronic re-dosing. ARCUS uses the same chromosomal excision as CRISPR but operates as a single self-contained protein rather than CRISPR's two-component Cas9 + guide RNA system, a size advantage that enables two cutting components to be delivered within a single AAV vector.

Exhibit 11. PBGENE-DMD Mechanism of Action



Source: Precision Biosciences investor presentation

- The study will enroll ambulatory DMD patients harboring mutations spanning exons 45–55; first site activation is targeted for the first half of 2026, with initial multi-patient efficacy data (assessed via the percentage of near-full-length dystrophin protein in muscle biopsies) anticipated by year-end. Following supportive data from at least ten patients, Precision would seek an FDA meeting to discuss a regulatory alignment path forward.
- REGENXBIO's (RGNX-Q, NR) AAV programs encountered two significant setbacks in quick succession, raising broader questions about AAV genotoxicity risk. On January 28, FDA placed a clinical hold on RGX-111 (MPS I/Hurler syndrome) after identification of an intraventricular CNS tumor treated four years prior. The patient was asymptomatic, with the tumor found on routine brain MRI and subsequently resected. Critically, preliminary genetic analysis of the tumor detected AAV vector genome integration associated with overexpression of PLAG1, a known proto-oncogene on chromosome 8q12. This is among the clearest clinical signals to date of potential AAV insertional oncogenesis in a human patient – a long time concern with the AAV class.
- The mechanism at play is not capsid-specific but rather reflects a fundamental property of rAAV vectors: while the vast majority of delivered DNA remains episomal, low-frequency random genomic integration events do occur, and when such integration lands near a proto-oncogene, the vector's enhancer/promoter elements can drive aberrant overexpression of that gene. PLAG1 activation via insertional mutagenesis has been demonstrated experimentally in retroviral models of hepatocyte transformation, producing a 20-fold increase in PLAG1 expression (Oncogene, 2014), and the PLAG gene family has independently been identified in a novel class of pediatric CNS embryonal tumors (*Keck et al., Acta Neuropathologica, 2023*).
- For the DMD landscape, the read-through is nuanced: RGNX is also developing RGX-202, an IV-administered AAV8-based gene therapy for DMD with pivotal data expected in Q2 2026. While RGX-202 uses a different capsid and delivery route than the intracisternal AAV9 programs on hold, the insertional mutagenesis risk is a property of the vector class rather than any individual capsid, and the regulatory overhang from the MPS findings could weigh on FDA's review posture for all AAV programs, including Precision Biosciences. For Satellos, the RGNX episode reinforces a key element of the MSCL thesis: SAT-3247 is a small molecule with no viral vector component, eliminating AAV-associated safety risks (immunogenicity, hepatotoxicity, insertional mutagenesis) entirely while offering the convenience of oral, chronic dosing.

- Compass reported positive topline results from its second pivotal Phase III trial. NY-based Compass Pathways (CMPS-Q, NR) reported data from the 581-patient COMP006 trial, focused on testing the firm's synthetic psilocybin formulation COMP360 in treatment-resistant depression (TRD; treatment-resistant usually means no longer responsive to selective serotonin reuptake inhibitor [SSRI] drugs). Two 25mg doses administered three weeks apart demonstrated a -3.8 point improvement on the Montgomery-Asberg Depression Rating Scale (MADRS) versus the 1mg control arm at Week 6

(p<0.001), with 39% of the 25mg cohort achieving a clinically meaningful response (defined as a 25% or greater reduction from baseline).

- These results are consistent with the first Phase 3 trial (COMP005; n=258), where a single 25mg dose achieved a -3.6 MADRS delta versus placebo (p<0.001) reported in June 2025. Compass has requested a meeting with the FDA to discuss a rolling NDA submission, targeting Q4 2026. If approved, COMP360 would be the first classic psychedelic cleared for use in the U.S. and would compete with J&J's (JNJ-NY, NR) Spravato (esketamine), which generated $1.7B in sales in 2025. Compass announced a US$150M equity offering after reporting COMP006 data, with timing clearly consistent with data quality & the positive regard ascribed to that quality by capital markets

- **Ocular reported topline results from its SOL-1 Phase III wet AMD trial.** MA-based ocular disease drug developer Ocular Therapeutix (OCUL-Q, NR) reported Phase III data from its wet age-related macular degeneration (wet AMD) trial (the 344-patient SOL-1 trial) testing its lead formulation AXPAXLI, an intravitreal tyrosine kinase inhibitor (axitinib) hydrogel implant, for the indication. The trial compared a single dose of AXPAXLI to a single dose of aflibercept 2mg (Regeneron's [REGN-Q, NR] Eylea) following a loading phase. Axitinib is actually already FDA-approved as a renal cell carcinoma drug, branded as Inlyta by CT-based pharma giant Pfizer (PFE-NY, NR). Because of axitinib's broader inhibitory activity on VEGF receptors specifically & on angiogenesis (new blood vessel growth) in general, it has long been plausible for innovators to explore the drug's utility in other dysregulated angiogenesis indications, of which wet AMD is one. Pfizer's FQ425 revenue for the drug, presumably for oncology indications alone, was US$235M (full-year F2025 revenue was US$923M).

  - The primary endpoint was met: 74.1% of AXPAXLI patients maintained visual acuity (<15 ETDRS letter loss) at Week 36 versus 56.6% in the aflibercept arm (risk difference 17.5%; p=0.0006). The Week 52 secondary endpoint was also significant, with 65.9% vs. 44.8% maintaining vision (risk difference 21.1%; p<0.0001). Critically, however, OCUL shares fell approximately 23% on the day. The market reaction reflects investor disappointment that the aflibercept control arm performed substantially better than anticipated, compressing the margin of superiority well below expectations.

Capital Markets Summary

Exhibit 12. EBITDA Or EPS-Positive Canadian Healthcare Stocks

Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 19-Feb	Mkt Cap (M)	Mkt Cap (C$M)	Ent. Value (M)	Ent. Value (C$M)	EV/EBITDA (T12M)	EV/EBITDA FY1	EV/EBITDA FY2	Price/Earnings (T12M)	Price/Earnings FY1	Price/Earnings FY2
Profitable Canadian healthcare firms - specialty services [2]														
dentalcorp Holdings	CAD	DNTL	192.0	$11.00	2,112	2,112	#N/A	#N/A	NA	NA	NA	NA	NA	NA
DRI Healthcare Trust	CAD	DHT.UN	55.1	$16.06	884	884	1,300	1,300	8.4x	5.9x	5.7x	NA	7.1x	5.7x
Jamieson Wellness	CAD	JWEL	41.3	$37.78	1,559	1,559	1,998	1,998	13.9x	10.9x	9.9x	25.3x	16.3x	14.4x
K-Bro Linen	CAD	KBL	13.0	$35.79	465	465	766	766	8.6x	7.0x	6.7x	21.5x	15.7x	11.8x
Medical Facilities [1]	CAD	DR	17.8	$11.90	211	289	396	543	6.8x	6.6x	6.9x	7.8x	12.5x	12.7x
Microbix Biosystems	CAD	MBX	138.6	$0.24	33	33	30	30	NA	NA	10.5x	NA	NA	NA
Savaria	CAD	SIS	71.7	$25.00	1,793	1,793	1,999	1,999	11.4x	10.0x	9.1x	28.9x	18.6x	15.9x
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales [2]														
Aurinia Pharmaceuticals	USD	AUPH	131.8	$14.31	1,887	2,584	1,607	2,201	10.8x	7.3x	6.1x	24.8x	15.3x	13.4x
Bausch Health	USD	BHC	370.9	$6.19	2,296	3,144	31,457	43,080	6.9x	6.1x	6.4x	6.3x	1.5x	1.6x
BioSyent	CAD	RX	11.5	$14.80	170	170	147	147	10.3x	11.7x	10.4x	19.4x	17.0x	15.6x
Cipher Pharmaceuticals [1]	CAD	CPH	25.3	$10.72	271	371	380	520	18.9x	14.9x	11.6x	15.8x	18.0x	13.4x
HLS Therapeutics	CAD	HLS	31.3	$4.50	141	141	201	201	9.0x	6.5x	5.6x	NA	NA	NA
Knight Therapeutics	CAD	GUD	98.7	$6.55	647	647	635	635	12.3x	9.7x	10.0x	NA	NA	46.8x
Medexus Pharmaceuticals	CAD	MDP	32.3	$2.85	92	92	107	107	5.7x	4.9x	3.6x	NA	NA	8.9x
Profitable Canadian healthcare firms - eldercare services or infrastructure developers														
CareRx	CAD	CRRX	62.8	$3.82	240	240	306	306	11.0x	7.8x	7.0x	NA	21.2x	15.3x
Chartwell Retirement Residences	CAD	CSH.UN	316.6	$22.12	7,004	7,004	9,587	9,587	25.7x	19.6x	17.8x	NA	NA	58.2x
Extendicare	CAD	EXE	94.5	$24.83	2,345	2,345	2,517	2,517	15.2x	11.6x	10.3x	23.1x	22.0x	18.7x
Northwest Healthcare Properties REIT	CAD	NWH.UN	250.0	$5.92	1,480	1,480	5,334	5,334	20.6x	22.2x	21.7x	29.6x	NA	NA
Nova Leap Health	CAD	NLH	87.3	$0.34	30	30	32	32	12.3x	NA	NA	39.1x	NA	NA
Sienna Senior Living	CAD	SIA	99.3	$23.40	2,324	2,324	3,553	3,553	24.9x	17.9x	16.5x	52.2x	40.3x	34.4x
Profitable Canadian healthcare firms - medical equipment distribution/sales														
Covalon Technologies	CAD	COV	27.6	$1.60	44	44	29	29	10.7x	6.3x	5.4x	21.3x	13.3x	11.4x
Quipt Home Medical [3]	USD	QIPT	44.0	$3.60	158	217	377	516	NA	4.2x	3.9x	NA	NA	NA
Viemed Healthcare	USD	VMD	38.0	$8.42	320	320	455	623	7.3x	4.7x	4.1x	24.1x	17.9x	13.6x
Profitable Canadian healthcare firms - healthcare IT or digital IT services firms														
Healwell AI	CAD	AIDX	294.1	$0.62	182	182	259	259	NA	28.1x	16.8x	NA	NA	NA
Hydreight	CAD	NURS	53.4	$3.98	212	212	202	202	NA	13.4x	5.8x	NA	14.2x	8.0x
Kneat.com	CAD	KSI	95.8	$4.06	389	533	359	359	NA	23.6x	16.4x	NA	NA	NA
Vitalhub	CAD	VHI	63.2	$8.06	510	698	388	388	17.8x	11.5x	9.8x	NA	32.6x	22.2x
Well Health	CAD	WELL	254.7	$3.93	1,001	1,001	1,697	1,697	16.4x	8.1x	7.3x	NA	9.5x	10.0x
Average									**13.0x**	**11.2x**	**9.4x**	**24.2x**	**17.2x**	**17.6x**
Recently-acquired Canadian healthcare firms														
Andlauer	*CAD*	*AND*	*39.2*	*$54.97*	*2,152*	*2,152*	*2,165*	*2,165*	*13.4x*	*NA*	*NA*	*32.0x*	*NA*	*NA*
Theratechnologies	*CAD*	*TH*	*46.0*	*$4.47*	*206*	*206*	*238*	*238*	*12.3x*	*NA*	*NA*	*NA*	*NA*	*NA*

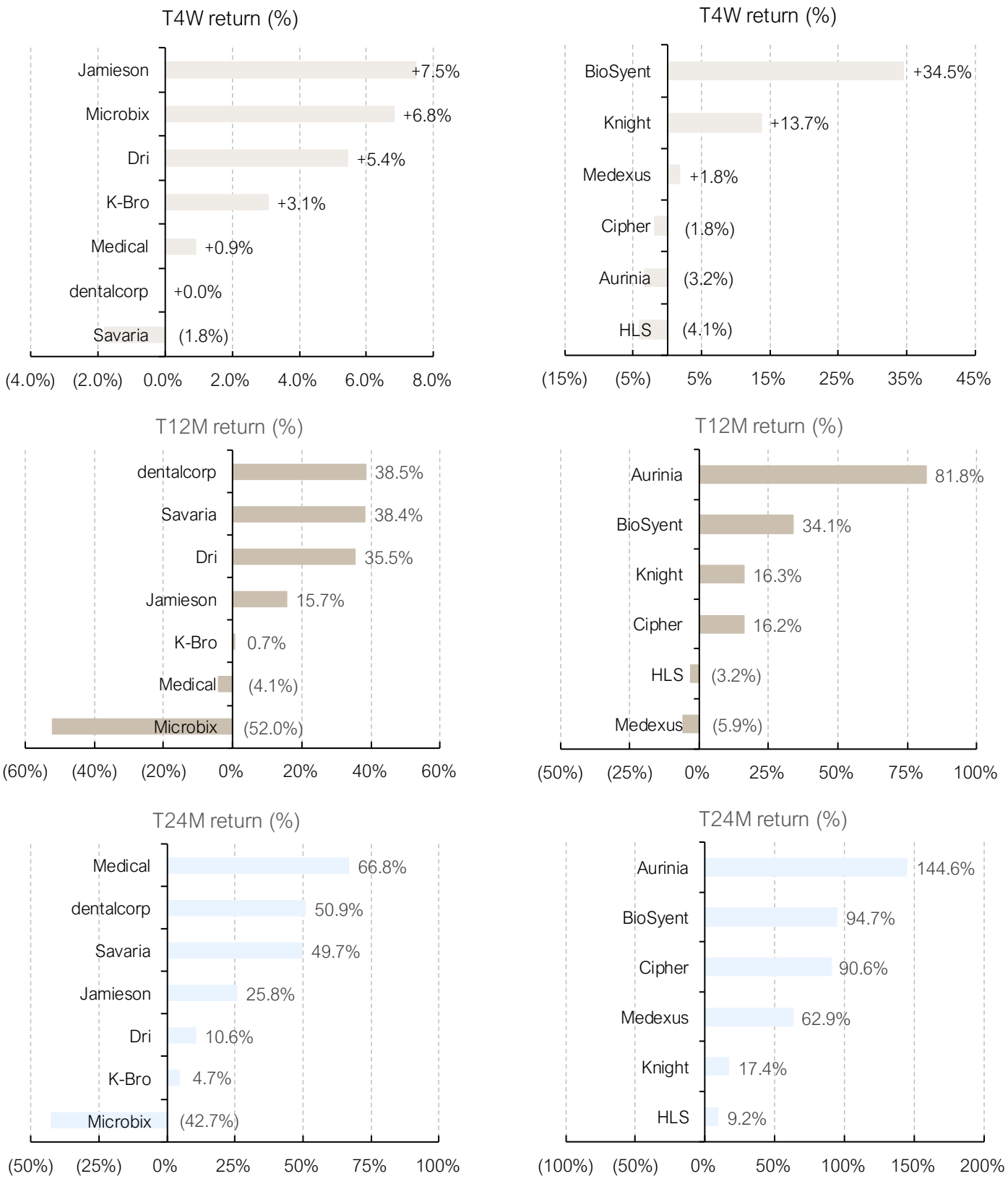
[1] Share price converted to USD for stocks reporting financial data in USD but for which share value is reported in CAD; price refers to prior day close, EV calculations based on cash/LT debt reported in most recent quarter

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

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

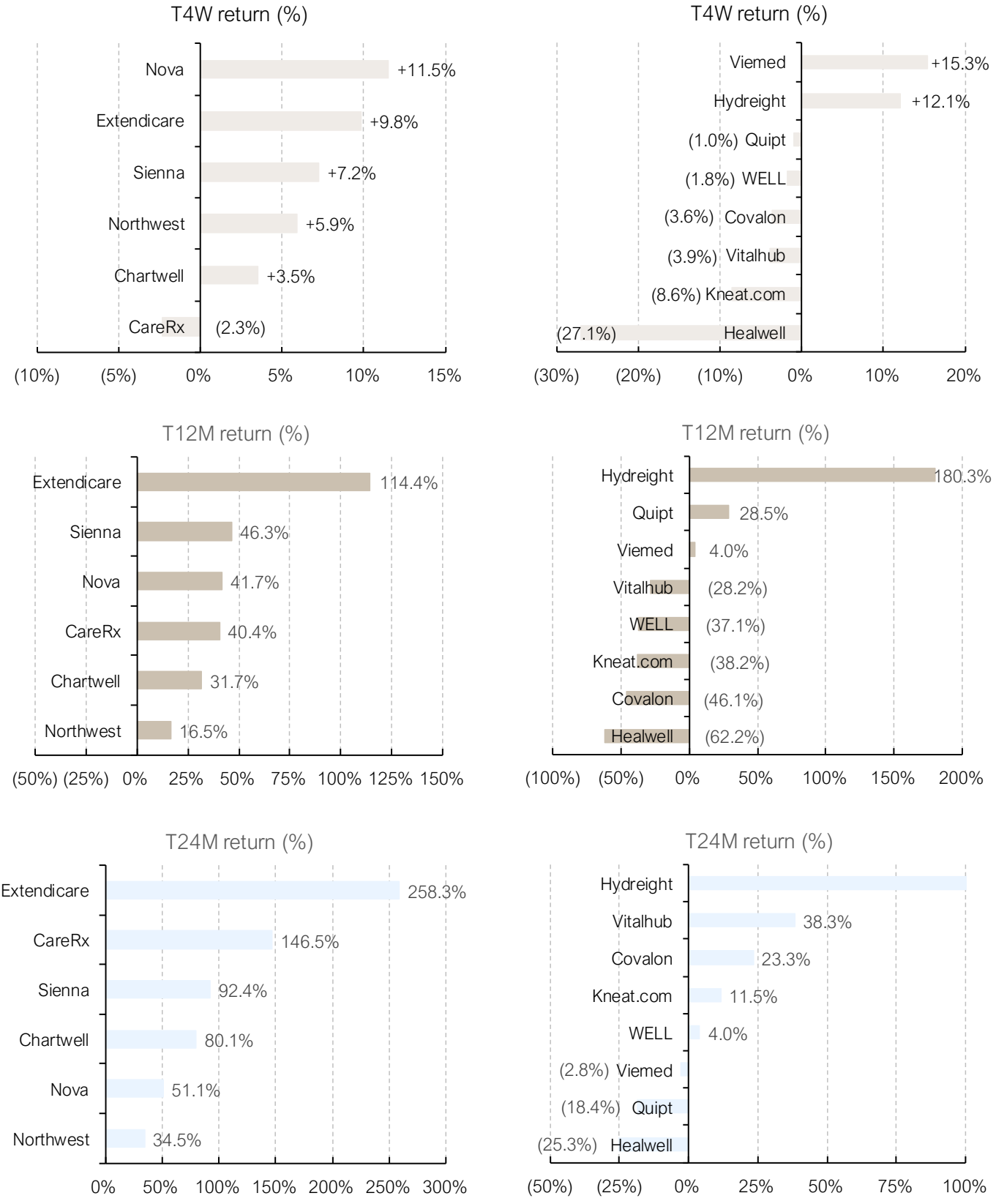
Source: Refinitiv, company reports, Leede Financial

Exhibit 13. 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 14. 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 1,144%)*

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RECOMMENDATION	NO. OF COMPANIES	%
Buy	9	56%
Speculative Buy	5	25%
Hold	1	6%
Sell	-	-
Tender	1	6%
Under Review	1	6%

Historical Target Price

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