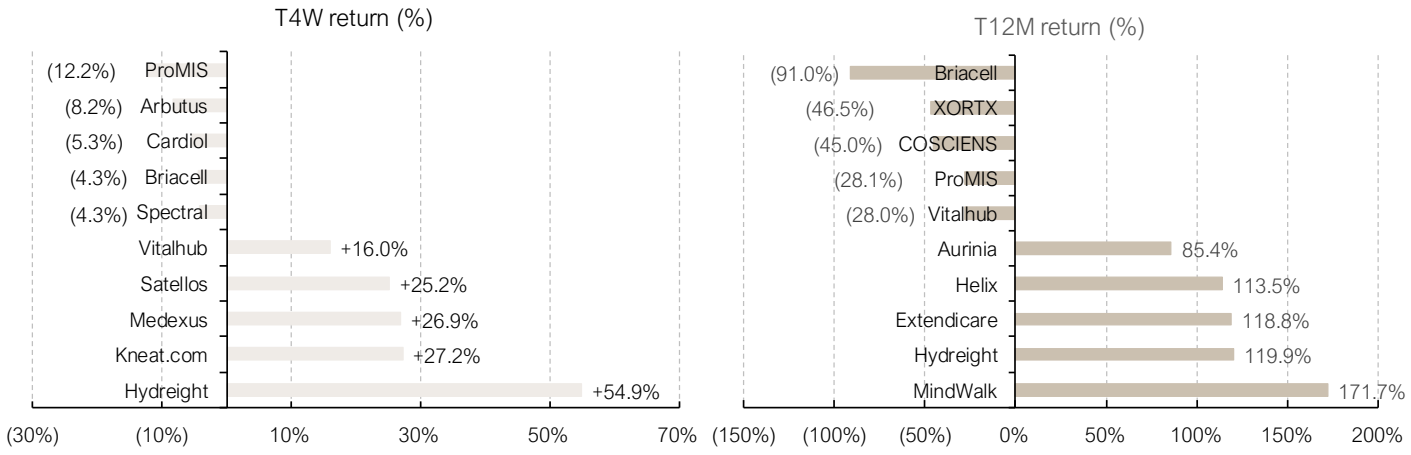
Core Highlights of the Week

Top Movers

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



Source: Leede Financial, Refinitiv

Updates From Our Healthcare Universe

- **Oncolytic establishes clinical path forward for pelareorep in squamous cell anal cancer.** CA-based cancer-focused biologics developer Oncolytics Biotech (ONCY-Q, Spec Buy, PT US$3.00) provided an update earlier this week on its clinical strategy for pelareorep, the firm's proprietary anti-cancer reovirus formulation, in targeting second-line squamous cell anal cancer (SCAC), a comparatively new indication in our conceptualization of pelareorep's medical prospects but an indication for which competitive landscape is fairly sparse & for which standard-of-care is stopgap at best.
  - The update was actually a bit less detailed than we anticipated in the wake of the firm participating in a formal consultation with the US FDA during which clinical details would have been comprehensively discussed. What we do know is the both Oncolytics & the FDA are in agreement that a biologic as comprehensively tested in multiple cancer indications as pelareorep is would not benefit from yet another single-arm exploratory trial.
  - Accordingly, we infer from Oncolytics' press release earlier this week that a controlled randomized SCAC trial should be funded, perhaps comparing pelareorep with standard-of-care therapy (Incyte's anti-PD1 mAb retafanlimab/Zynyz, [FQ126 sales US$41.4M] in combination with carboplatin & paclitaxel, on which we have more to say below). Coincidentally, retafanlimab/Zynyz (with carboplatin/paclitaxel) was approved in Europe just weeks ago in Mar/26 for treating first-line SCAC, further confirming this biologic as a leading component of SCAC standard-of-care.
  - Recall that Oncolytics is in fact testing pelareorep as a SCAC therapy in the ongoing 122-patient GOBLET trial in which a proportion of patients in the gastrointestinal cancer-focused trial presented with third-line SCAC at enrollment. Patients were already refractory to at least two courses of prior chemotherapy & so were not solely platinum-resistant as we expect patients to be in the new SCAC trial that Oncolytics is contemplating but data are still useful as a benchmark for future testing in our view. In this trial, pelareorep is combined not with retafanlimab/Zynyz but with

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Roche's (ROG-SW, NR) anti-PD-L1 mAb atezolizumab/Tecentriq that while not the same mAb of course does still intercede at through the immunologically-relevant PD1/PD-L1 checkpoint inhibition pathway. In a press release published earlier in FQ126, Oncolytics reported that of the fourteen evaluable third-line SCAC patients in the trial, objective response rate was 29% & median duration of response was 17 months.

Exhibit 2. Income Statement & Financial Forecast Data For Oncolytics Biotech, F2025A-to-F2036E

Year-end December 31 *(US$M, except per share data)*	2025A	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
Pelareorep royalty revenue, by indication												
Breast cancer	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$19.6	$63.2	$86.9	$111.6
Pancreatic cancer	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$5.4	$25.9	$51.1	$67.6	$84.7
Colorect cancer, second-line	$0.0	$0.0	$0.0	$0.0	$0.0	$6.7	$38.3	$82.3	$109.5	$137.8	$167.2	$197.7
Squamous cell anal cancer	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.5	$2.3	$4.9	$7.0	$8.5	$10.0
Royalty rev, pelareorep	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$6.7**	**$38.8**	**$90.0**	**$160.0**	**$259.1**	**$330.2**	**$404.1**
Revenue growth (%)	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*478%*	*132%*	*78%*	*62%*	*27%*	*22%*
Payments from future partners	$0.0	$0.0	$5.0	$7.5	$7.5	$7.5	$7.5	$7.5	$7.5	$7.5	$7.5	$7.5
SG&A expense (amortization-adj)	$13.3	$25.0	$25.0	$25.0	$25.0	$20.0	$15.0	$12.5	$10.0	$7.5	$5.0	$5.0
R&D expense	$12.2	$12.2	$12.2	$12.2	$12.8	$13.4	$14.1	$14.8	$15.5	$16.3	$17.1	$18.0
EBITDA	**($25.6)**	**($37.2)**	**($32.2)**	**($29.7)**	**($30.3)**	**($19.2)**	**$17.2**	**$70.2**	**$141.9**	**$242.8**	**$315.6**	**$388.6**
EBITDA growth (%)	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*407.2%*	*202.1%*	*171.1%*	*130.0%*	*123.1%*
EBITDA margin (%)	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*44.4%*	*78.0%*	*88.7%*	*93.7%*	*95.6%*	*96.2%*
Cumulative non-cash expenses	$3.2	$2.7	$2.7	$2.7	$2.7	$2.7	$7.0	$20.3	$38.2	$63.4	$81.6	$99.9
Net Income, fully-taxed	($28.9)	($40.0)	($35.0)	($32.5)	($33.1)	($22.0)	$10.1	$49.8	$103.6	$179.3	$233.9	$288.6
EPS (fully-taxed, basic)	($0.27)	($0.37)	($0.32)	($0.30)	($0.31)	($0.20)	$0.09	$0.46	$0.96	$1.66	$2.17	$2.67
EPS (fully-taxed, fd)	**($0.22)**	**($0.30)**	**($0.26)**	**($0.24)**	**($0.25)**	**($0.17)**	**$0.08**	**$0.37**	**$0.78**	**$1.35**	**$1.76**	**$2.17**
S/O (basic, M)	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*	*108.0*
S/O (fully-diluted, M)	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*	*132.9*
P/E	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*11.9x*	*2.4x*	*1.2x*	*0.7x*	*0.5x*	*0.4x*
EV/EBITDA	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*5.4x*	*1.3x*	*0.7x*	*0.4x*	*0.3x*	*0.2x*

Source: Oncolytics Biotech financial filings, Leede Financial

- Without context, it is challenging to determine just how positive Oncolytics' SCAC response rate data in GOBLET actually are, but we ourselves are favorably disposed to that magnitude of tumor response in this difficult-to-treat cancer form that until Incyte came along with retifanlimab, few oncology drug developers chose to focus on this indication. In the 2025 *Lancet* paper in which POD1UM-303 data were described, Incyte provided some anal cancer epidemiology data that was consistent with data embedded into our model, but bear repeating here.

Exhibit 3. Valuation Scenarios for Oncolytics Biotech

NPV, discount rate		20%	25%	30%	35%	40%	50%
Implied value per share		$8.96	$5.49	**$3.36**	$2.01	$1.15	$0.21
				Discounted share price end-of-2026			
Price/earnings multiple, F2033	**P/E**	**20%**	**25%**	**30%**	**35%**	**40%**	**50%**
Implied share price[1]	10	$2.61	$2.04	$1.61	$1.29	$1.03	$0.68
	20	$5.22	$4.08	**$3.23**	$2.58	$2.06	$1.36
	30	$7.83	$6.12	$4.83	$3.87	$3.09	$2.04
EV/EBITDA multiple, F2033		**5x**	**7.5x**	**10x**	**12.5x**	**15x**	**17.5x**
Implied share price[1,2]		$1.12	$1.67	$2.22	$2.78	$3.33	$3.88
One-year ONC target price (US$)				**$2.94**			

[1] *Based on F2033 fd fully-taxed EPS forecast of $0.78; EBITDA of $141.8M; 30% discount rate*

[2] *EV based on FQ425 cash of US$5.2, no LT debt, S/O (fd) of 132.9M (basic S/O 108.0M)*

[3] *PT derived from projections in CDN, converted to USD using USD:CDN ratio of 1.37x*

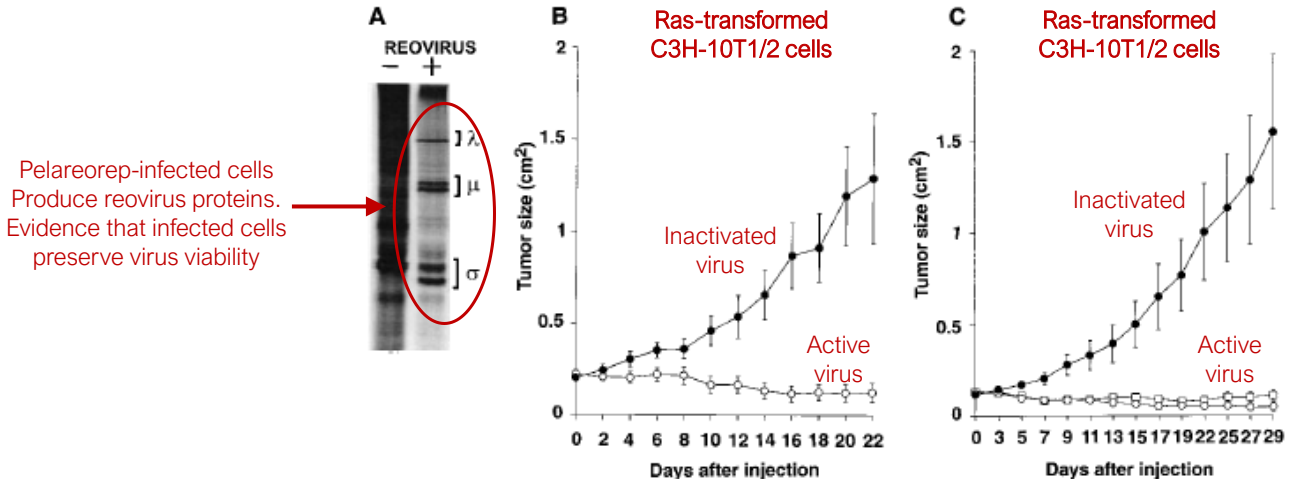
Source: Oncolytics Biotech financial filings, Leede Financial

- As cited in the 2025 Lancet paper indicated above, about 14% of anal cancer cases are already metastatic when diagnosed (unlike, for example, breast or colorectal cancer for which CT or endoscopic screening is more common) & even localized disease will progress nearly 40% of the time even after localized radiation therapy combined with platinum-based chemotherapy (though chemotherapy based on retifanlimab-carboplatin-paclitaxel is likely to displace legacy chemotherapy [which in the EU was carboplatin-paclitaxel] on which these epidemiology data were based).

- According to a 2021 review published in the *Journal of Experimental Pharmacology*, SCAC represents a small but measurable 2.5% of all GI cancer forms (with colorectal cancer in all its stages & forms being the dominant GI cancer indication). First-line chemotherapy until recently was a combination of localized radiation plus an infusion of the drugs 5-fluorouracil, capecitabine & mitomycin, all of which work at the level of indiscriminately disrupting DNA replication & repair. HPV infection is frequently associated with SCAC biology & therapies/vaccines that target the most oncologically-relevant HPV strains could be relevant in SCAC standard-of-care to be sure. But Oncolytics is targeting second-line patients for which HPV-targeted drugs/biologics were unable to prevent disease onset. HIV infection is also a strong predictor of SCAC risk (incidence is 25x-to-35x higher than in HIV-negative individuals), but highly-active anti-retroviral therapy is not generally considered to exhibit anti-cancer activity, at least not after cancer symptoms have already emerged.

- Indeed, Oncolytics explicitly refers to retifanlimab in its press release this week, citing the now-completed 94-patient platinum-refractory second-line SCAC trial (the POD1UM-202 trial, published in the journal *ESMO Open* in 2022) that was a single-arm retifanlimab monotherapy trial & thus differs in both respects from study design that we expect Oncolytics to adopt but one where objective absolute patient performance established a foundation at which further clinical testing would be justified. In POD1UM-202, objective response rate to retifamlimab monotherapy was 13.8%, disease control rate (so including patients with stable disease in this analysis) was 48.9%, with median duration of response of 9.5 months & progression-free survival/overall survival of 2.3 months & 10.1 months, respectively.

Exhibit 4. Reovirus/Pelareorep's Anti-Tumor Activity In Ras-Transformed Tumors Is Well-Documented & In Fact Forms The Basis For Oncolytics' Creation As A Publicly-Traded Cancer-Focused Biologics Developer



Panel C, open squares – previous exposure to reovirus (which leads to production of anti-reovirus Abs) does not limit anti-tumor activity of subsequent reovirus/pelareorep administration

Source: Adapted by Leede Financial from *Science (1998). Vol. 282, pp. 1332-1334*

- But these values are just values without context & retafamlimab innovator Incyte (INCY-Q, NR) did fund a much larger controlled Phase III SCAC trial (this time in first-line patients who were not yet treated with platinum-based drugs) that was published in Jun/25 in *The Lancet*. In the predictably-labeled POD1UM-303 trial, 376 first-line patients were randomized to receive retafamlimab in combination with carboplatin & paclitaxel, with the latter microtubule-binding drug coincidentally performing well in combination with pelareorep in a few legacy Phase II studies (metastatic advanced breast cancer & pancreatic cancer). In that trial, for which the control arm was carboplatin/paclitaxel alone, progression-free survival in the retafamlimab arm was 9.3 months vs 7.4 months for control patients.

Exhibit 5. Historic & Pending Clinical Milestones For Pelareorep

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)
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 (interim 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 during H226
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	Possibly H127 (OS as primary endpoint)
Commence patient enrollment	Pivotal Phase III	Metastatic breast cancer (HER2-neg/ HR-pos), probably Enhertu-refractory	180	Paclitaxel	Unpartnered	Possibly H128 (PFS/OS as primary endpoint)
Commence patient enrollment	Phase II	Squamous cell anal carcinoma (second-line)	TBD	TBD, but possibly paclitaxel or Incyte's retifanlimab/Zynyz	Unpartnered	Expect trial activation during H226

Source: Oncolytics Biotech financial filings, tabulated by Leede Financial

- **Summary & valuation.** We are encouraged by Oncolytics resolve in picking a lane on pelareorep clinical development & affirming that its previous decision to focus on gastrointestinal cancer forms (including second-line platinum-resistant Kras mutation-harboring microsatellite-stable colorectal cancer, as our model also assumes & as indicated in Exhibit 5), including squamous cell anal cancer for which CA-based drug developer Incyte has singularly re-defined standard-of-care with retifanlimab/Zynyz.
    - There are still some gaps in our understanding of Oncolytics' SCAC study design but we make some evidence-based assumptions on pelareorep/SCAC clinical elements & regardless, our model assumes now as before that a Phase II/III SCAC trial incorporating pelareorep-retifanlimab-carboplatin-paclitaxel in some combination will commence enrollment some time during FH226.
    - We are maintaining our Speculative Buy rating & one-year PT of US$3.00 on ONCY, with our valuation still based on NPV (30% discount rate) & multiples of our F2033 EBITDA/fd EPS forecasts of US$141.8M & US$0.78/shr, respectively. Importantly though, we are clear in our legacy Oncolytics commentary as we are here that the firm will need to identify sources of funds either from capital markets or cash-contributing partners to drive pending Phase II/III pelareorep clinical programs forward & we will watch for advances on this theme in coming months.
- **Cardiol updates clinical status for its MAvERIC/recurrent pericarditis pivotal trial.** ON-based small-molecule cardiovascular disease drug developer Cardiol Therapeutics (CRDL-T, Spec Buy, PT C$7.00) provided an update on patient enrollment status for its pivotal 110-patient Phase III recurrent pericarditis trial (the MAvERIC trial) testing its ultrapure orally-active cannabidiol formulation CardiolRx in patients with prior therapy with Kiniksa Pharmaceuticals' (KNSA-Q, NR) interleukin-1-blocking biologic rilonacept/Arcalyst (FQ126 sales US$214.3M; F2026 guidance of US$930M-to-US$945M, so sequential growth still expected to continue).
    - The update while positive is more evolutionary than revolutionary in our outlook on CardiolRx's medical prospects in this larger-than-anyone-thought-it-was cardiovascular infectious disease market, with Cardiol striving to accelerate timelines to data through adding new enrolling centers for MAvERIC, centers that we infer from the US NIH's clinical database

(where several new centers are now indicated as not-yet-recruiting) includes Johns Hopkins University, the Minneapolis Heart Institute, the University of Utah Hospital & four new hospitals in Italy in Milan-Torino-Padua-Udine. There is always a modest risk to accelerating patient enrollment in any Phase III trial through expanding enrolling centers just because variability in regional standards-of-care can introduce variability in patient outcomes or in how disease is diagnosed or staged even for a comparatively easy-to-diagnose indication like recurrent pericarditis or for an easy-to-administer orally-active therapy like CardiolRx/cannabidiol. Moreover, patient inclusion criteria are about as self-defining as for any Phase III clinical program we have monitored in our drug development coverage history, in this case with eligible patients presenting with pericarditis symptoms that were originally but are no longer responsive to rilonacept/Arcalyst treatment.

Exhibit 6. Income Statement & Financial Forecast Data For Cardiol, F2026E-to-F2035E

Year-end December 31 *(C$000, exc per share data)*	*2026E*	*2027E*	*2028E*	*2029E*	*2030E*	*2031E*	*2032E*	*2033E*	*2034E*	*2035E*
CardiolRx (Acute Myocarditis)	$0	$0	$0	$0	$0	$33,573	$84,436	$101,932	$136,724	$171,931
CardiolRx (Recurrent Pericarditis)	$0	$0	$0	$32,597	$81,981	$107,214	$116,154	$125,198	$125,949	$126,705
CardiolRx (injectable, diast HF)	$0	$0	$0	$0	$0	$42,954	$86,424	$108,678	$131,196	$153,981
CardiolRx (COVID-19)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total revenue	**$0**	**$0**	**$0**	**$32,597**	**$81,981**	**$183,742**	**$287,015**	**$335,807**	**$393,869**	**$452,616**
Revenue growth (%)	*NA*	*NA*	*NA*	*NA*	*252%*	*224%*	*156%*	*117%*	*117%*	*115%*
R&D, clinical expenses	$7,500	$5,000	$5,123	$5,248	$5,377	$5,508	$5,643	$5,782	$5,923	$6,068
G&A, marketing expenses	$16,041	$15,765	$15,495	$16,537	$17,847	$20,240	$21,660	$20,964	$21,894	$22,843
Other expenses	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
EBITDA	**($23,541)**	**($20,765)**	**($20,618)**	**$10,812**	**$58,757**	**$157,993**	**$259,711**	**$309,062**	**$366,052**	**$423,704**
EBITDA growth (%)	(5%)	(12%)	(1%)	(152%)	443%	169%	64%	19%	18%	16%
EBITDA margin (%)	*NA*	*NA*	*NA*	*33%*	*72%*	*86%*	*90%*	*92%*	*93%*	*94%*
Non-operating expenses	$719	$719	$719	$719	$719	$719	$719	$719	$719	$719
EBIT	**($24,260)**	**($21,484)**	**($21,337)**	**$10,093**	**$58,038**	**$157,274**	**$258,992**	**$308,343**	**$365,333**	**$422,985**
Other non-oper expenses	$384	$384	$384	$384	$384	$384	$384	$384	$384	$384
EBT	**($24,643)**	**($21,867)**	**($21,721)**	**$9,709**	**$57,655**	**$156,891**	**$258,609**	**$307,960**	**$364,950**	**$422,602**
Tax expense	$0	$0	$0	$2,913	$17,296	$47,067	$77,583	$92,388	$109,485	$126,781
Net income, fully-taxed	($24,643)	($21,867)	($21,721)	$6,796	$40,358	$109,823	$181,026	$215,572	$255,465	$295,821
Fully-taxed EPS (basic)	($0.25)	($0.22)	($0.22)	$0.07	$0.40	$1.10	$1.81	$2.15	$2.55	$2.95
Fully-taxed EPS (fd)	**($0.22)**	**($0.19)**	**($0.19)**	**$0.06**	**$0.36**	**$0.97**	**$1.60**	**$1.91**	**$2.26**	**$2.62**
P/E (basic)	*NA*	*NA*	*NA*	*29.7x*	*5.0x*	*1.8x*	*1.1x*	*0.9x*	*0.8x*	*0.7x*
EV/EBITDA	*NA*	*NA*	*NA*	*14.6x*	*2.7x*	*1.0x*	*0.6x*	*0.5x*	*0.4x*	*0.4x*
S/O, basic (M)	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*	*100,257*
S/O, fd (M)	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*	*112,919*

Source: Cardiol Therapeutics financial filings, Leede Financial

- If new centers can each contribute one or two patients to final data analysis, we are optimistic that Cardiol can achieve its goal of enrolling >110 patients into MAvERIC probably by early FQ326, a reasonable target both for Cardiol & for our model with the trial already meeting 75% of target enrollment. Assuming that target enrollment is achieved over that timeline, Cardiol & its collaborators could accumulate efficacy data from all patients by FQ127 & perhaps report data in press release or medical abstract form by FQ227.

- The trial commenced in Apr/25 & thus would already have generated efficacy data from early enrollees, though with the trial clearly still blinded to investigators. Recall that MAvERIC's primary endpoint is fairly straightforward by Phase III standards & is assessing pericarditis recurrence rate, impact on circulating C-reactive protein (a general marker of systemic inflammation) & impact on the eleven-point Numeric Rating Scale pain score at six-month follow-up, all of which are endpoints by which CardiolRx performed well in the completed 27-patient MAvERIC-Pilot trial completed in 2024, with data presented at the American Heart Association annual meeting in Nov/24.

- Summary & valuation. We are maintaining our PT/rating on CRDL, with our valuation still based on NPV (25% discount rate that we believe is appropriate for a Phase III-stage drug developer, with investment thesis-validating Phase II data already available for our review) & multiples of our F2031 adjusted EBITDA/fd EPS forecasts of C$158.0M & C$0.97/shr, respectively. As an aside, we continue to reflect favorably on just how ubiquitously cannabidiol now is described in the medical literature as being relevant to treating various cardiovascular indications, not just recurrent pericarditis or acute myocarditis or heart failure (see below). The most recent commentary on this theme was just published in Feb/26 by Mayo Clinic researchers in the clinic's own journal Mayo Clinic Proceedings; we reproduce two notable exhibits from that review in Exhibit 8.

Exhibit 7. Valuation Scenarios for Cardiol

NPV, discount rate		10%	20%	25%	30%	40%	50%
Implied value per share		$22.22	$9.99	**$6.54**	$4.78	$2.67	$1.20
Price/earnings multiple, 2031E		**10%**	**20%**	**25%**	**30%**	**40%**	**50%**
Implied share price[1]	**10**	$7.02	$4.95	$4.21	$3.60	$2.39	$2.03
	20	$14.04	$9.90	**$7.13**	$7.20	$4.78	$4.06
	30	$21.06	$14.85	$12.63	$10.80	$7.17	$6.09
EV/EBITDA multiple, 2031E		**5x**	**10x**	**12.5x**	**15x**	**17.5x**	**20x**
Implied share price[1,2]		$3.12	$6.32	**$7.92**	$9.52	$11.13	$12.73
One-year Cardiol target price (C$) [1]				**$7.20**			

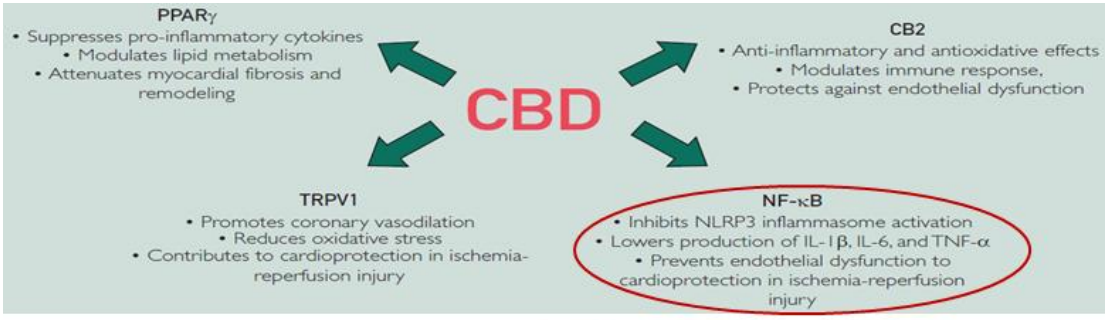
[1] *Based on F2031 fully-taxed EPS of $0.97; EBITDA of $158.0M, discounted at 25%, FD S/O of 112.9M, including Oct/25 equity offering*

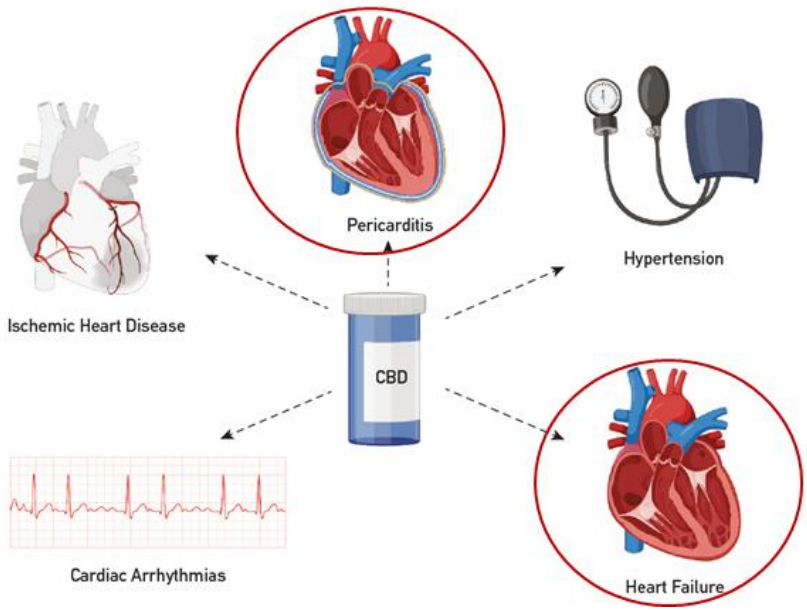
[2] *Includes FQ425 cash of $21.4M, no LT debt*

Source: Cardiol Therapeutics financial filings, Leede Financial

- Though the firm separately presented data from its Phase II acute myocarditis trial (the ARCHER trial) that was mechanism-validating if not quite at a statistically significant performance level on key endpoints, our model still ascribes value to acute myocarditis as a tertiary indication, with diastolic heart failure (or also called heart failure with preserved ejection fraction, a heart pathology where the left ventricle does not fill with oxygenated blood from the left atrium as efficiently as it should; HFpEF) representing a seminal secondary market in our model.

Exhibit 8. Cannabidiol's Medical Prospects In Cardiovascular Disease Are More Widely Recognized In Recent Peer-Reviewed Publications, Undoubtedly Driven In Part By Cardiol's Own Advances With CardiolRx/CRD38





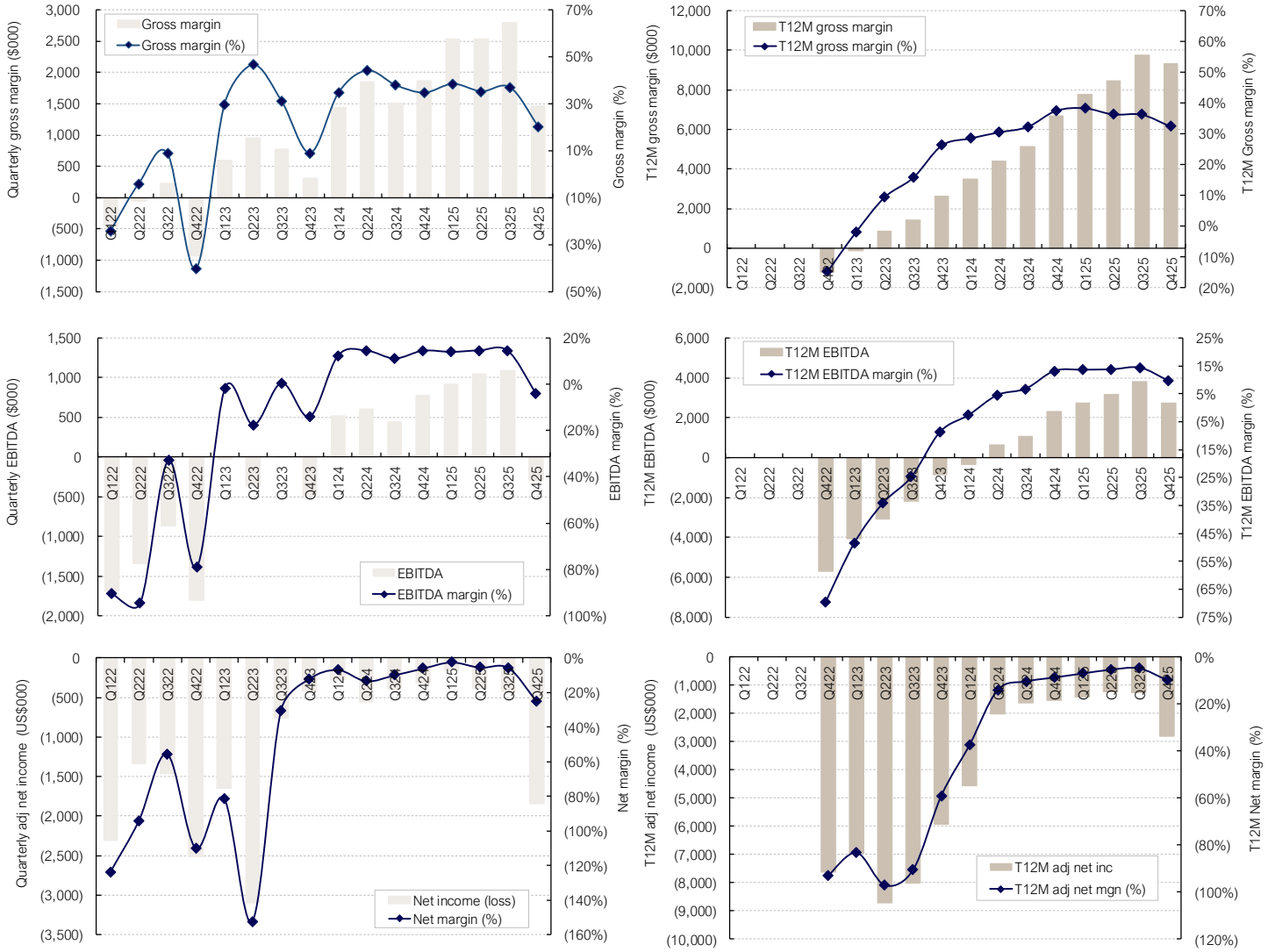
Source: Adapted from *Mayo Clinic Proceedings (2026). Vol. 101, pp. 297-309*

- For this indication, Cardiol developed a subcutaneously-injectable polyethylene glycol-elastin-line polypeptide-based cannabidiol formulation called CRD38 for which validating preclinical data were published last year in the *Journal of the American College of Cardiology*. Our model assumes that IND-enabling CRD38 studies are ongoing & that Phase I HFpEF/CRD38 clinical testing can commence by end-of-F2026. But for now, our attention is squarely focused on MAvERIC & on timelines to data in this large & growing medical market that peer firm Kiniksa has shown to have blockbuster potential.

Other Significant Clinical Trial Updates With Relevance To Our Coverage Universe

- **LSL Pharma reports FQ425 financial data – negative adjusted EBITDA quarter is clearly cautionary but is already a fading memory with multiple F2026 product launches on the horizon.** QC-based topical cosmetics & pharmaceutical products manufacturer LSL Pharma (LSL-V, NR) reported FQ425 financial data for the long-ago-concluded December-end period that were soft both in absolute terms & in comparison to trailing quarters, with a litany of one-time items negatively impacting gross margin (which we back out of our own gross margin calculation) & a gain on acquisition corresponding to the acquisition of Laboratoire Du-Var in Nov/25 that negatively impacted operating cash flow as calculated by the firm itself but which we will for our own purposes allocate to investing activity in the exhibits that follow.

Exhibit 9. Quarterly & T12M Gross Margin-EBITDA-Net Income Data For LSL Pharma, FQ122-to-FQ425

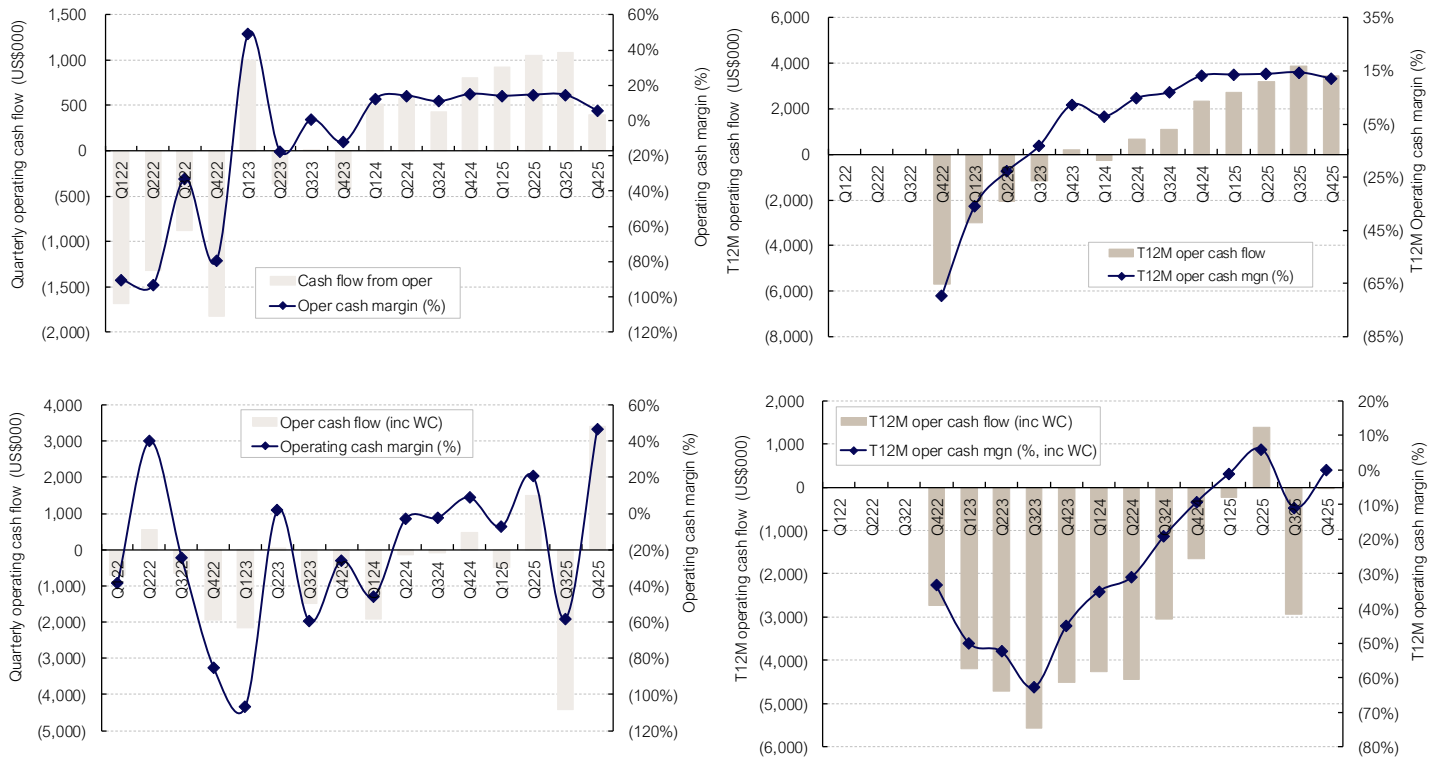


Source: LSL Pharma financial filings, Leede Financial

- After our own re-interpretation of LSL's financial data, the quarter was still soft on adjusted gross margin-EBITDA-operating cash flow, but the firm should benefit from quarterly contribution from six new Health Canada-approved topical products for which we inferred product characteristics from the Health Canada Therapeutic Products database & described in an earlier edition of our Healthcare Weekly. New approvals includes the glaucoma-targeted alpha-2-adrenoceptor agonist drug brimonidine tartrate, other glaucoma drugs in carbonic anhydrase inhibitor dorzolamide & a dorzolamide combination with beta-adrenergic receptor blocker timolol, the prostaglandin analog latanoprost & a latanoprost-timolol combination drug, plus the allergic conjunctivitis-targeted selective histamine H1 antagonist drug olopatadine. In the FQ425 MD&A, LSL indicated that the cumulative market size in Canada for these six glaucoma/conjunctivitis products in aggregate is $66M, though the firm did not provide any product-specific revenue guidance.

- LSL's existing portfolio includes erythromycin for which LSL's Steri-Med division received health Canada approval back in May/21, along with the anti-bacterial aminoglycoside drug gentamycin (approved in Feb/25), another broad-spectrum anti-bacterial agent chloramphenicol (approved in Mar/25), the sulfacetamide/prednisolone combination therapy Dioptimyd (approved in Apr/25), two different bacitracin/polymyxin B anti-bacterial formulations branded as Pink Eye Ointment & Sterisporin (approved in Dec/21 & May/17). This legacy portfolio is independent of the over-the-counter (OTC) portfolio that LSL acquired from private specialty pharmaceutical firm JUNO in Jan/26, for which F2026 cumulative sales are expected to be $25M.

Exhibit 10. Quarterly & T12M Cash Flow Data For LSL Pharma, FQ122-to-FQ425



Source: LSL Pharma financial filings, Leede Financial

- Shifting back to FQ425 financial data, which while soft on many metrics was still a transitional quarter for the firm with JUNO OTC products & newly-approved glaucoma/conjunctivitis products expected to drive F2026-to-F2028 growth, the firm generated by our calculation revenue/gross margin/EBITDA in the quarter of $7.3M/$1.47M/($0.3M) as compared sequentially to FQ325 data of $7.6M/$2.8M/$1.1M & y/y to FQ424 data of $5.4M/$1.87M/$0.78M. Gross margin was encumbered with a collection of one-time items – provisions for receivables related to US shortages of erythromycin from NY-based partner Fera Pharmaceuticals (private) along with a few inventory write-downs & R&D charges – that totaled US$2.35M & for our purposes we inserted into the income statement below the EBITDA line.

- EBITDA as reported was far more negative without that adjustment. As a thematic comment on LSL's FQ425 & F2025 financials, data were laden with multiple one-time charges that required extraction from as-reported data in order to assess financial performance of FQ425 foundational operations. The firm exited the quarter with cash of $0.5M & total debt of $30.1M; debt-based financial ratios are meaningless in a negative EBITDA quarter but for the record, EBITDA-to-interest coverage ratio in the preceding quarter was 2.0x while debt-to-FQ325 EBITDA run-rate ratio was 5.6x. Both ratios conferred modest financial risk for the firm based on our own risk stratification criteria that prefers to see these ratios well above 3x & well below 3x, respectively. But new product launches in F2026 should make trailing debt ratios irrelevant probably as soon as the trailing FQ126 period.

- Separately, we calculate that FQ425 pure operating cash flow was $0.4M, far less negative than as reported by LSL based on our decision to exclude impact from the Laboratoire Du-Var acquisition that we allocated to investing activities. Working capital was solidly into surplus territory in the quarter at $3.0M, bringing adjusted pure FQ425 operating cash flow by our calculation to $3.4M. Excluding working capital, FQ425 pure cash flow was still down sequentially from $1.1M in FQ325 & down y/y from FQ424 pure cash flow of $0.8M (in FQ424, we allocate impact from disposal of intangible assets of $4.9M in investing activities (it was incorporated into cash flow in LSL's own cash flow statement).

- **Sun Pharma acquires global pharma giant Organon.** India-based specialty pharmaceutical giant (& Cipher's Absorica marketing partner, as we will describe) Sun Pharma (524715-BSE, NR) is acquiring NJ-based peer Organon (OGN-NY, NR) in a deal valuing Organon at an EV of US$11.75B, corresponding to 6.2x EV-to-F2025 EBITDA of US$1.91B & 1.9x EV-to-F2025 revenue of US$6.22B. Interestingly, the transaction is not expected to close until early F2027.

  - Continuing with some more book-keeping on the transaction, Organon exited FQ425 with a modest cash balance of US$574M but with pro forma cash of US$1.1B augmented by US$440M in proceeds from Organon's divestiture of its intrauterine vacuum/post-partum uterine bleeding-hemorrhage device JADA to NH-based Laborie Medical Technologies (private) in Jan/26. Not to dwell on JADA too intensively, but total value ascribed to JADA on this divestiture (up to US$465M, including a pending US$24M milestone payment) was a substantial 6.3x multiple of F2025 JADA revenue of US$74M, with the product certainly growing but not unusually aggressively at 22% y/y.

  - **Valuation multiples look aggressive to us when ascribed to trailing economic data, implying that strategic value is a core component of transaction value.** Total F2025 debt of US$8.6B was high in comparison to core profitability metrics (see below) & thus with balance sheet data materially influencing the firm's EV in comparison to its implied market value of US$3.64B. Organon's debt-to-F2025 EBITDA ratio of 4.5x was quite high at the end of its last fiscal year & its F2025 EBITDA-to-interest coverage ratio of 3.8x was also high by the standards that we conventionally ascribe to EBITDA-positive, debt/interest-bearing firms in our coverage universe, including specialty pharmaceutical firms.

  - Sun/Organon's press release announcing the transaction did not emphasize any specific products in Organon's commercial portfolio that drove its interest in the acquisition, but on a thematic basis, Sun indicated that its own branded/generic/biosimilar franchise at a minimum exhibits additive if not synergistic overlap with Organon's Innovative Medicines operations, even before considering that Organon has its own suite of biosimilar therapies that should fit smartly into Sun's imminent focus on building out its own biosimilar franchise.

  - **Organon's women's health division generated limited growth in F2025 & actually experienced y/y revenue decline once now-divested JADA revenue is excluded.** Organon has a clear focus on women's health & features this therapeutic category in its investor presentations – leading drugs are related to fertility – either enhancing its probability or mitigating it – with contraception brands Nexplanon (etonogestrel implant)-Marvelon/Mercilon (oral desogestrel/ethinyl estradiol)-NuvaRing (etonogestrel/ethinyl estradiol vaginal ring) collectively generating F2025 sales of US$1.1B while fertility brands Follistem AQ (injectable follitropin beta)-Ganirelix (an injectable gonatotropin-releasing hormone antagonist) collectively generating US$365M in F2025 sales. The women's health portfolio, from which we exclude JADA, was actually down (2.2%) y/y, making the multiple ascribed to Organon in the Sun transaction looking a bit aggressive to us (Organon's biosimilar portfolio was up only by 4% y/y; see below).

  - **Organon's biosimilar portfolio did grow y/y in F2025 but not to a level that justifies the revenue multiple implied by the Sun acquisition offer.** Organon's suite of biosimilar therapies is already sizable by competitive standards, with the existing pipeline including Renflexis (a biosimilar of Johnson & Johnson/Centocor's [JNJ-NY, NR] ant-TNFα mAb infliximab/Remicade; F2025 sales US$251M but down [8%] y/y), Hadlima (a biosimilar anti-TNFα mAb for AbbVie's

[ABBV-NY, NR] adalimumab/Humira; F2025 sales US$228M, up 60% y/y), Ontruzant (a biosimilar anti-HER2 mAb for Roche/Genentech's [ROG-SW, NR] Herceptin; F2025 sales US$99M but down [30%] y/y), Brenzys (a biosimilar of Amgen's [AMGN-Q-NR] anti-TNF fusion protein Abetanercept/Enbrel; F2025 sales US$80M, up 4% y/y) & biosimilars of tocilizumab (a biosimilar of interleukin-6 receptor-targeted rheumatoid arthritis mAb Actemra as developed by Roche/Genentech [ROG-SW, NR]) & denosumab (a biosimilar of RANKL-inhibiting osteoporosis mAb Prolia/Zgeva as developed by Amgen [AMGN-Q, NR]) collectively generating modest sales so far of US$33M, up 17% y/y.

- Despite Organon's emphasis on women's health & biosimilar sales, a larger proportion of its F2025 Rx sales were derived collectively from other indications, including a cardiovascular portfolio (sales were US$1.13B, down [14%] y/y), non-opioid pain-dermatology-bone health drugs (sales were US$987M last year, up 14% y/y), respiratory therapies (sales were US$842M, down [17%] y/y) & a collection of other drugs/biologics collectively designated as Other Established brands (including regional rights to Eli Lilly's [LLY-NY, NR] calcitonin gene-related peptide-targeted anti-migraine mAb galcanezumab/Emgality) that were up 13% y/y. Collectively, sales for this collection of commercial Rx therapies was US$3.69B, down (4%) y/y. We will not stratify Organon's sales in these indications any further, other than to emphasize again that the firm was clearly generating solid revenue/EBITDA in absolute terms, but with little-to-no growth trajectory across its entire pharma footprint when collectively considered.

- **Probably minimal impact on Cipher, but for the record, Sun is Cipher's US marketing partner for Absorica.** Shifting to relevance to our coverage universe, Sun is of course the US distributor of Cipher Pharmaceuticals' (CPH-T, Buy, PT C$19.00) Lidose-based super-bioavailable orally-active cystic acne-targeted isotretinoin formulation Absorica, for which Cipher's quarterly royalty revenue (which was 7.5% of net sales by Sun; Cipher's manufacturing partner Galephar PR [private] received a comparable royalty under an original US distribution agreement with Ranbaxy Pharmaceuticals that was acquired by Sun in Apr/14) has been steadily declining since peaking at US$30.1M, achieving what our model assumes is a nadir in F2025 of only US$1.8M. Clearly Sun was a disinterested partner for this drug after years of being a quality partner in our view & the Organon acquisition is unlikely to intensify its interests in Absorica promotion going forward.

- Organon does have one dermatology-focused branded therapy in plaque psoriasis-targeted tapinarof formulation Vtama & Organon did feature Vtama as a seminal growth asset in its FQ424 corporate update in Feb/26. As we have emphasized in prior Cipher commentary, Cipher is contractually able to acquire US marketing rights from Sun by end-of-FQ426 & that quarter cannot transpire fast enough in our view. The drug is separately sold in Canada by Cipher itself as Epuris, where sales continued to climb based in our view on the formulation's superior PK profile (no food effects on GI absorption for this fairly water-insoluble retinoid analog) is resonating with Canadian dermatologists. Cipher sells Epuris at a comparable price to generic isotretinoin alternatives & we believe that Sun continues to sell Absorica at a premium to the multiple generic forms currently available in the US. We believe that Cipher will independently revisit Absorica's US pricing strategy when it assumes responsibility over all commercial activities for the drug.

- In our view, the Sun-Organon transaction is unlikely to have a material impact on Absorica quarterly royalty revenue that was already at trough levels, so our model assumes, nor should it have an impact on timelines on Cipher's contractual ability to assume US marketing rights for the drug. Cipher has US marketing infrastructure now that it is marketing its head lice/scabies-targeted Spinosad formulation Natroba & thus is better positioned to assume US marketing responsibilities for Absorica or any other dermatology-focused Rx asset it may seek to license/acquire down the road. For now, we are maintaining our PT/rating on CPH.

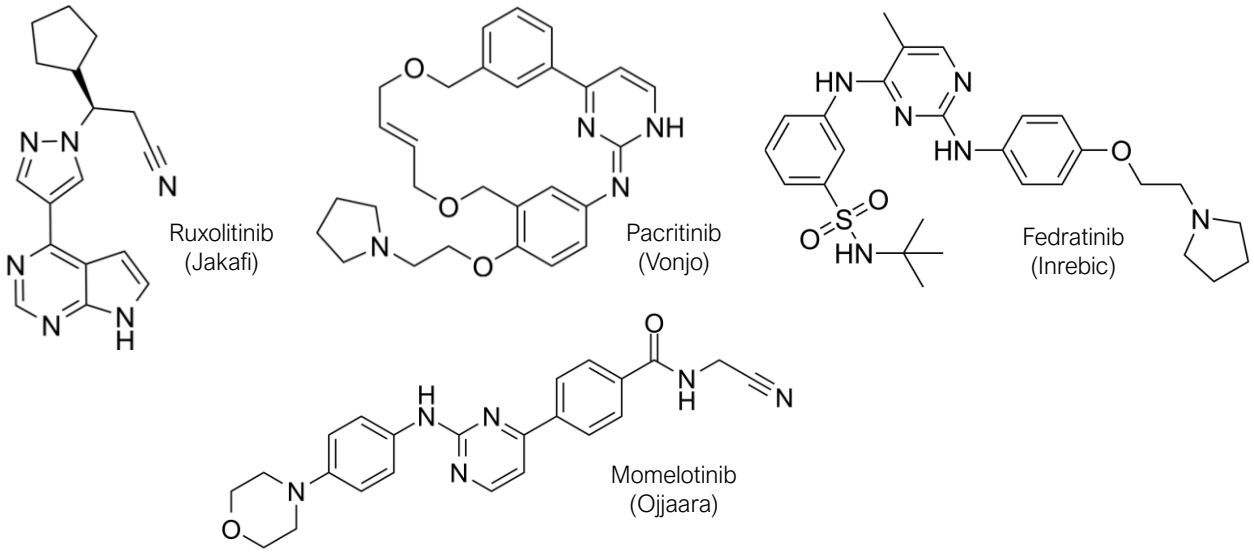
- **Eli Lilly acquires myelofibrosis therapy developer Ajax, compelling us to reflect nostalgically on how this indication once impacted our coverage universe more overtly.** IN-based global pharma giant Eli Lilly (LLY-NY, NR) acquired myelofibrosis therapy developer Ajax Therapeutics in a deal valuing Ajax at up to US$2.3B through an unstratified combination of upfront capital & future clinical/regulatory milestones that are undoubtedly tied to achieving positive Phase III myelofibrosis data & FDA approval thereafter.

  - Ajax's lead drug is **AJ1-11095**, a small-molecule inhibitor of the protein JAK2 (short for Janus kinase 2), a tyrosine kinase enzyme that if mutated, makes hematopoietic cells in the body more sensitive to other hormones that simulate red blood cell production, like erythropoietin. At present, Ajax is actively enrolling patients in a 76-patient Phase I/II trial, for which PK data & 26-to-52-week impact on spleen volume or Total Symptom Score are expected by early F2027. Importantly, one of the trial's key enrollment criteria is that patients must have either been unresponsive to, or relapsed

after, prior treatment with another FDA-approved JAK2 inhibitor drug (we describe a few competitive drugs below), thus establishing a key niche for AJ1-11095 if it performs well in the ongoing trial.

- AJ1-11095's molecular structure is not published in the medical literature so we do not have any insights into what structural motifs in the drug could be relevant to how it impacts JAK2-relevant pathways in myelofibrosis that are not mitigated by other already-approved JAK-targeted drugs. As we show in Exhibits 11 & 12, the structural diversity of both FDA-approved & clinical-stage myelofibrosis drugs is vast & so few insights on AJ1-11095 molecular characteristics are available to us from reviewing pharmacology of alternative myelofibrosis drugs developed by Ajax's peers. Ajax does have a core US patent issued last year for which the title (*6-Heteroaryloxy Benzimidazoles & Azabenzimidazoles* As JAK Inhibitors) obviously provides us with some insights into what AJ1-11095's structural elements could be, though imidazole drugs tend to be anti-fungal agents, a functionality that is unlikely to be relevant to JAK2 inhibition.

Exhibit 11. FDA-Approved JAK Inhibiting Myelofibrosis Drugs



Source: *Company reports, MedChemExpress*

- Indeed, Ajax reported mechanism-confirming preclinical data at the American Society of Hematology meeting in Dec/25 that presumably motivated Eli Lilly's interests in AJ1-11095, showing that AJ1-11095 was able to restore inhibition of JAK-mediated pathways in JAK2 mutation-harboring cell types that were refractory to another JAK2 inhibitor, Incyte's **ruxolitinib/Jakafi** (see below). AJ1-11095 was also superior to ruxolitinib/Jakafi in JAK2-mutation-harboring myelofibrosis mouse models on reducing spleen volume & improving overall bone marrow physiology.

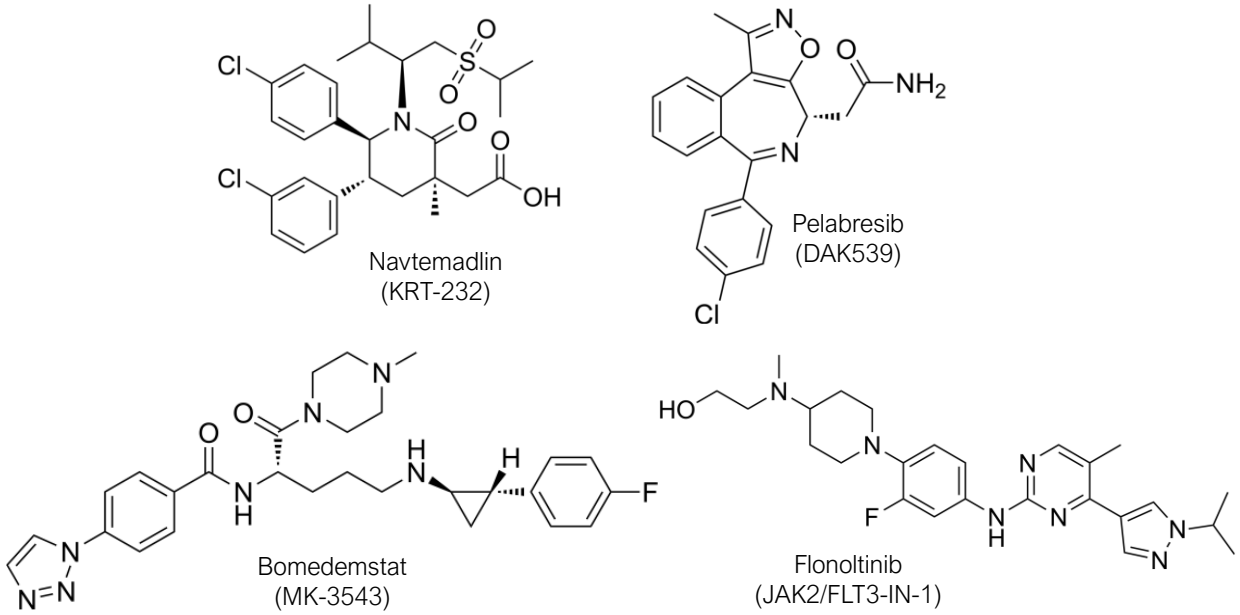
- The timing of the transaction is interesting to us not just for the intrinsic characteristics of the drug itself but more because of the competitive status of this still-Phase I clinical asset when considering all of the Phase III-stage myelofibrosis drugs that could generate their own efficacy data in the next few years, even before considering the existing JAK2 inhibitor pharmacopeia. As Ajax reported in various poster presentations, most other JAK-targeted myelofibrosis drugs only bind to active conformations of JAK2 & so over time, myeloproliferative neoplastic (MPN) cells in bone marrow lose their response to such drugs over time, creating a pharmacologic justification for alternative JAK-targeted drugs that do not bind exclusively to active JAK2 conformations, which AJ1-11095 does.

- Not all of these are JAK2 inhibitors though & this target has already been shown itself to be highly-druggable, mostly through the success of Incyte Pharmaceuticals' (INCY-Q, NR) ruxolitinib/Jakafi (F2025 sales US$3.1B & FQ126 sales just reported of US$758M; an atopic dermatitis-targeted ruxolitinib cream formulation Opselura separately generated US$678M in sales last year as well & US$143M in FQ126) & also by Bristol Myers Squibb's JAK2 & FMS-like tyrosine kinase 3 (FLT3)-inhibitor **fedratinib/Inrebic**, though impairment charges on this drug recorded in BMS' F2024 annual report of US$280M suggest to us that Inrebic sales have been more modest than for Jakafi (indeed, F2025 Inrebic sales

were not explicitly quantified by BMS in its F2025 10K filing, though it was part of a portfolio of 'other growth products' that collectively generated US$1.9B last year).

- That physiological disruption thus leads to overproduction of red blood cells & corresponding disruption of organs in the body that store or reprocess red blood cells as well, such as the spleen. Inhibiting JAK2 thus mitigates the pathways through which JAK2 acts that have a direct role in regulating red blood cell production; indeed, there are a family of hematopoietic disorders for which red blood cell dysregulation is a key pathology & these include the indications myelofibrosis as stated above, as well as two other indications called polycythemia vera & essential thrombocythemia.
- Myelofibrosis specifically is estimated (we are citing data that GlaxoSmithKline [GSK-LN, NR] published in its F2025 annual report) to afflict one in 500,000 individuals worldwide (& about 20,000 individuals in the US alone, according to Ajax) & so is clearly an orphan indication (Ajax received Orphan Drug Status from the US FDA in Dec/25), yet with Incyte clearly showing that effective therapies can achieve blockbuster status for an indication that is underserved by previous standard-of-care, regardless of its population prevalence.

Exhibit 12. Clinical-Stage Myelofibrosis Drugs, Including Candidates That Do Not Directly Inhibit JAK-Based Pathways

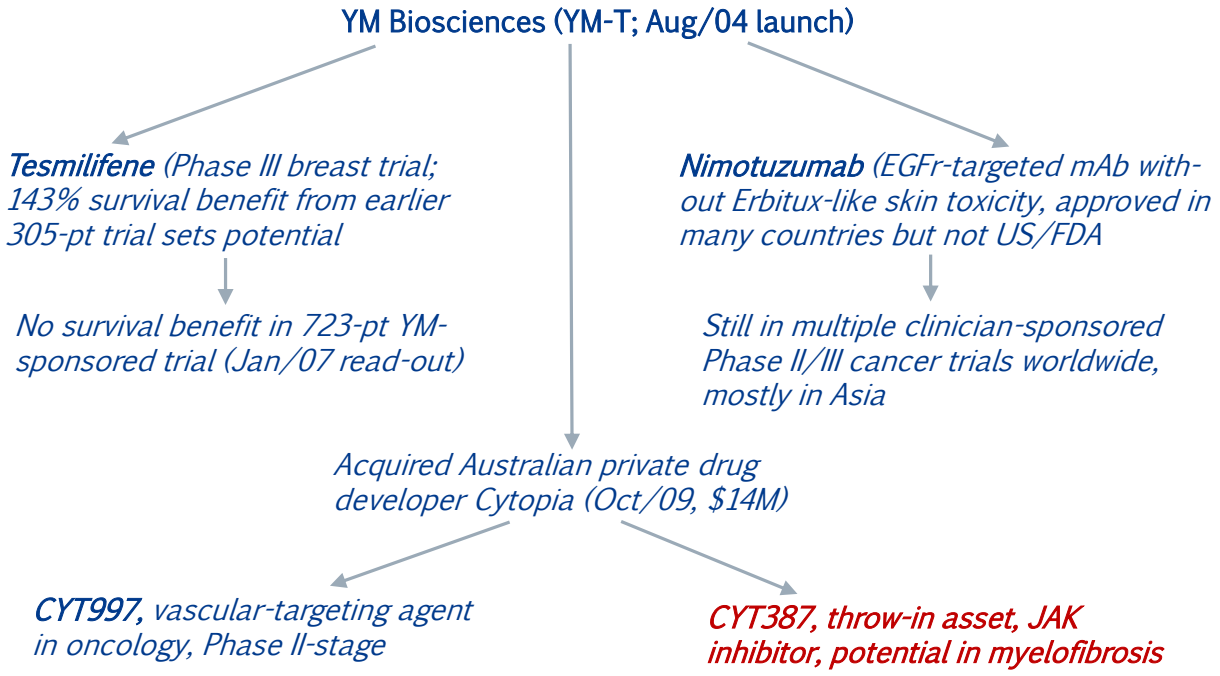


Source: *Company Reports, MedChemExpress, US NIH clinical trials database*

- Starting with myelofibrosis, this is actually a form of bone marrow cancer that by residing in the bone marrow is anatomically related to multiple myeloma though with distinct symptoms & modes of therapy. For myelofibrosis, as the name implies, manifests itself with scarring/fibrosis within bone marrow but like the other indications we mentioned above, it is initially diagnosed through the overproduction of red blood cells that it causes. Even though JAK2 is a common target for many myelofibrosis drugs that have been FDA-approved in recent years (see Exhibit 11), other mutations in the genes encoding calreticulin (a calcium-regulating protein within cells that normally plays a role in protein folding pathways but a key secondary role is that it can be expressed on the surface of cells that are destined for programmed cell death).
- Accordingly, cells that do not express calreticulin on their cell surface are not recognized by the body as being primed for reprocessed & thus just continue to grow in a cancerous way & thrombopoietin receptor (this receptor as expressed in the kidneys & liver regulates production of blood platelets when bound to thrombopoietin, but it is also expressed in karyocytes in bone marrow where if mutated, it becomes constitutively activated to over-produce platelets) are separately relevant to disease onset.

- It is difficult to target calreticulin with myelofibrosis drugs because its absence & not its presence is associated with disease progression, but mutated thrombopoietin receptor can in fact be targeted by structural analogs of thrombopoietin that impede the ability of thrombopoietin itself to bind to the receptor. Approved thrombopoietin receptor-targeted drugs include Amgen's romiplostim/Nplate & Novartis' (NVS-NY, NR) eltrombopag/Promacta, but both drugs predictably target platelet-overproduction diseases (thrombocytopenia or a related disorder called idiopathic thrombocytopenic purpura) & not red blood cell-overproducing disorders like myelofibrosis that is relevant to the Lilly-Ajax transaction.

Exhibit 13. History Is Contingent & Proceeds Most Often In A Non-Linear Path – And So Does Drug Development (Part One)



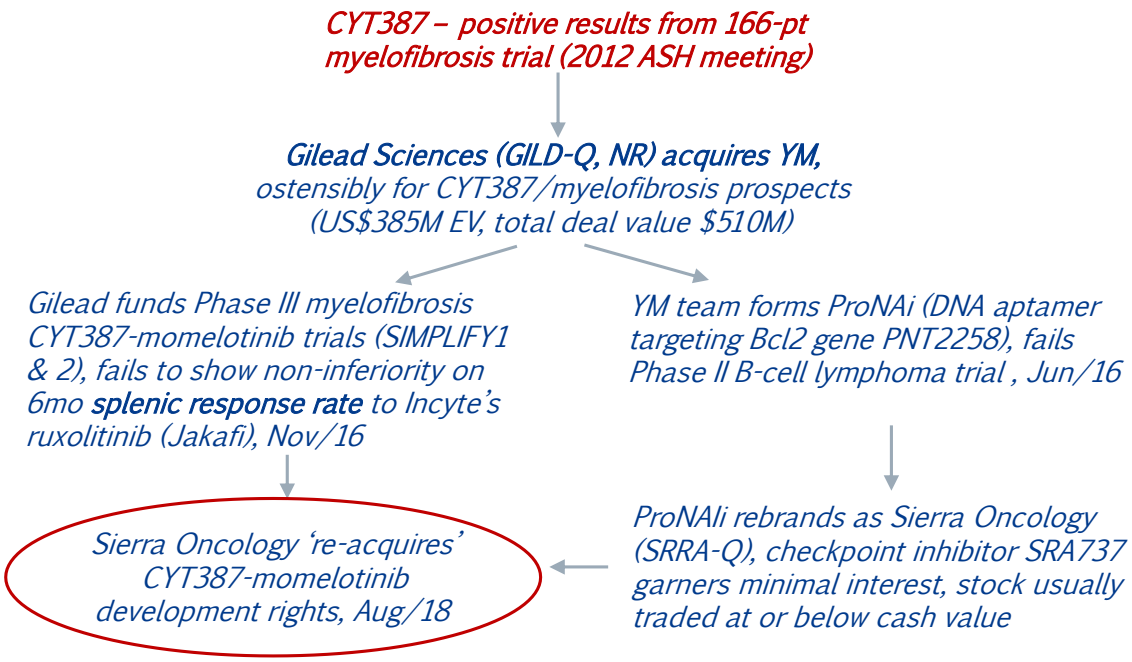
Source: *Company reports, Leede Financial*

- But shifting back to myelofibrosis, there are in fact two related but distinct pathologies that tend to be monitored as part of diagnosing disease progression or of determining efficacy of experimental therapies. One marker of disease is that myelofibrosis patients exhibit enlarged spleens so one endpoint in clinical trials can be to assess impact on spleen volume reduction. Another key symptom is duration of transfusion independence because ironically, one of the manifestations of this red blood cell-overproducing disease is anemia, implying that overproduction of red blood cells leads not to excessive oxygen-carrying capacity of such cells but an impaired ability to do so. There are a few Phase III myelofibrosis drugs in advanced clinical testing & these include:
  - Swedish Orphan Biovitrum (SOBI-STO, NR) already-FDA-approved (in 2022) JAK2-specific inhibitor drug **pacritinib/Vonjo** (F2025 sales SEK1.242B/US$135M) but for which supplemental testing in the 399-patient PACIFICA trial is ongoing (final data on six-month transfusion independence & spleen volume changes are expected by H227).
  - CA-based Kartos Therapeutics (private) is testing MDM2-inhibiting **navtemadlin/KRT-232** in combination with Incyte's ruxolitinib/Jakafi in myelofibrosis patients with no prior JAK inhibitor therapy in the 600-patient POIESIS trial, for which six-month spleen volume reduction & total symptom score data are expected by end-of-F2028. MDM2 is short for mouse double minute 2, a name that is a bit of an inside joke reference to how the protein was discovered & in what species (in a mouse cell line called 3T3-DM), but moving on from nomenclature, the protein is part of a family of proteins called E3 ligases that generally facilitate protein turnover & degradation but in the case of MDM2, its specific role is to inhibit the DNA-repairing tumor suppressor protein p53 by tagging it for degradation. By

inhibiting MDM2 as navtemadlin does, it lifts the biological tumor suppression that p53 confers. This study was described in a paper published just a few weeks ago in the journal *Future Oncology*.

- Imago BioSciences/Merck's (MRK-NY, NR) lysine-specific demethylase 1 (LSD1) inhibitor drug **bomedemstat** is undergoing Phase III testing in a disease-diverse hematologic disorder 400-patient trial for which ten-year impact on disease remission in a patient subset with polycythemia vera & myelofibrosis are expected by F2034. A separate suite of Phase III thrombocythemia trials (the 300-patient Shorespan-007 & the 340-patient Shorespan-006 trial) are both expected to generate three-year fatigue symptom score data by F2028. Merck's interests in bomedemstat development are clearly not focused exclusively on myelofibrosis or polycythemia vera, but we will still be interested to see if at final data analysis if there is some measure of efficacy in this indication & how that might compare to future AJ1-11095 myelofibrosis clinical data.

Exhibit 14. History Is Contingent & Proceeds Most Often In A Non-Linear Path – And So Does Drug Development (Part Two)



Source: *Company reports, Leede Financial*

- Morphosys/Novartis' (NVS-NY, NR) **pelabresib/DAK539** is undergoing testing in combination with ruxolitinib/Jakafi in a 460-patient Phase III myelofibrosis trial (the MANIFEST-3 trial) for which six-month spleen volume reduction & total symptom score data are expected by end-of-F2030. Positive spleen volume reduction data at six-month follow-up were previously reported for pelabresib/ruxolitinib in the Phase II 430-patient MANIFEST-2 trial, as published in May/25 in *Nature Medicine*. The drug is not a JAK2 inhibitor as so many approved myelofibrosis drugs are, as AJ1-11095 is predicted to be as well, but rather it is an orally-active small-molecule inhibitor of a so-called bromodomain & extra-terminal (BET) protein.

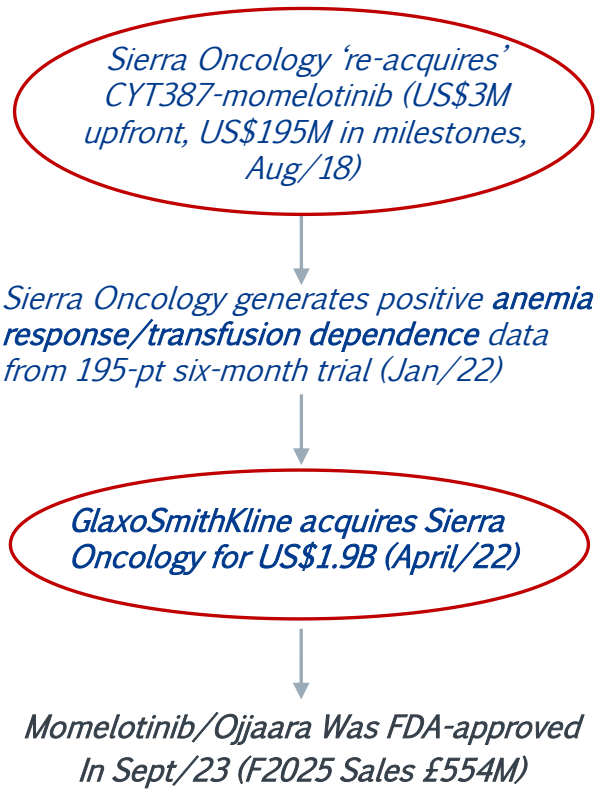
- BET is a family of proteins that, as the name implies, contain so-called bromodomains that have the ability to find side chains on the amino acid lysine within histone proteins (specifically histones H3 & H4) to which acetyl groups are attached. By recognizing these regions, BET proteins can impact the activity of transcription factors (so proteins that mediate encoding of RNA from a defined DNA sequence) that themselves recognize acetylated H3/H4 regions. Many BET inhibitor drugs are in formal clinical testing, most of which are targeting more conventional cancer indications & not myelofibrosis, though a few are (obviously including pelabresib/DAK539).

- **Ropeginterferon alfa-2b/P1101 (BESREMi)** is an interferon formulation that is already FDA-approved for treating polycythemia vera & is undergoing testing in a 150-patient Phase III myelofibrosis trial (the HOPE-PMF trial) sponsored by Taiwan-based PharmaEssentia (6446-TW, NR) at a single site in Japan, for which final 80-week total

symptom score data are expected by end-of-F2028. Even though BESREMi is already approved in a few geographies for targeting polycythemia vera, a separate 111-patient Phase III trial targeting polycythemia vera is expected to generate data by H227.

- Bristol Myers Squibb' (BMY-NY, NR) activin receptor-based transforming growth factor-beta (TGF-β)-binding fusion protein **luspatercept/Reblozyl** is already FDA-approved as an erythroid maturation agent for targeting beta-thalassemia & myelodysplastic syndrome (MDS); F2025 sales were US$2.3B, mostly in the US. It is undergoing Phase III testing in myelofibrosis in a 196-patient trial in China sponsored by Guangzhou-based Nangang Hospital/Southern Medical University for which final data are expected by end-of-F2030.

Exhibit 15. History Is Contingent & Proceeds Most Often In A Non-Linear Path – And So Does Drug Development (Part Three)



Source: *Company reports, Leede Financial*

- The JAK2 inhibitor **flonoltinib maleate** is undergoing testing by the China-based firm Zenitar (private) in a 105-patient Phase III myelofibrosis trial for which final spleen volume reduction & transfusion independence data are expected by mid-F2028. Interestingly, like so many early-stage drug developers in our world, Zenitar features an AI-based structural biology platform that forms the basis for its lead identification programs, including presumably for flonoltinib maleate discovery. Like AJ1-11095, flonoltinib maleate was granted FDA Orphan Drug Status. A 75-patient Phase II trial that is comparing flonoltinib to ruxolitinib is separately ongoing (the protocol was published last month in the journal *Therapeutics Advances in Hematology*) & poised to generate six-month spleen volume reduction data in H226. The drug is already approved in China.
- Belgium-based University Hospital Brest is funding an anticoagulation drug combination in **apixaban/rivaroxaban** (Bristol Myers Squibb's [BMY-NY, NR] Factor Xa Eliquis & Janssen Pharmaceuticals' [JNJ-NY, NR] Factor Xa inhibitor Xarelto) as a way to mitigate thrombo-embolic events (blood clots) that can arise in disease states for which the underlying cause is overproduction or dysregulation of red blood cell production, including but not limited to myelofibrosis & polycythemia vera. The 1,308-patient trial (AVAJAK trial) is comparing two-year thrombotic event rate to patients receiving low-dose acetylsalicylic acid (ASA) as an alternative anti-coagulation drug & data on event rate is expected by H227.

- Clearly an anti-coagulation therapy, which as an aside has no real probability of not reducing thrombotic event rate in comparison to placebo but comparisons to ASA-treated patients could be insightful, is not addressing the underlying causes of myelofibrosis & related disorders & so we would not consider this program to be overly meaningful to AJ1-11095's medical prospects. Interestingly though, the trial is exclusively enrolling patients harboring a specific mutation in the JAK2 protein (a phenylalanine-for-valine substitution at position #617 of JAK2's amino acid chain), so the trial does have some relevance, if indirectly, to JAK2 physiology.

- So why are we emphasizing a drug development alliance that is targeting an indication for which there is no current relevance to our coverage universe? Because it once did many years ago & in a way that reminds us just how non-linear the path to medical product commercialization can be. This narrative reflects strikingly on a legacy coverage stock of ours (ON-based small-molecule & biologics developer YM Biosciences [ticker was YM-T]) & how it eventually created value with a legacy JAK1/2-inhibiting myelofibrosis-targeted small-molecule drug now branded by GlaxoSmithKline (GSK-LN-NR) as momelotinib/Ojjaara.

- The drug was a secondary asset in the portfolio of a cancer-focused drug developer that YM acquired nearly seventeen years ago now & as history has shown, it became the most valuable in YM's portfolio, or at least it was once an appropriately-designed clinical trial under stewardship of the right entrepreneurs became a reality in Ojjara's clinical/regulatory activities. The relevant timelines are as described in Exhibits 13-to-15 & the respective figures are excerpted from a presentation that we shared with our Leede Financial partners at a corporate retreat back in Sept/23.

- **Intellia reports positive Phase III hereditary angioedema data for lonvo-z, validating *in vivo* CRISPR clinically but leaving differentiation versus established regimens up for debate.** Positive topline results were reported by MA-based Intellia Therapeutics (NTLA-Q, NR) from the HAELO trial this week. HAELO is a randomized, double-blind, placebo-controlled Phase III trial evaluating lonvoguran ziclumeran, or lonvo-z, as a one-time in vivo CRISPR/Cas9 therapy for Type I/II hereditary angioedema. HAELO enrolled 80 adults & adolescents aged 16 years & older, randomized to a single 50 mg IV infusion of lonvo-z (n=52) or placebo (n=28). The study met its primary endpoint, with lonvo-z reducing mean monthly HAE attack rate by 87% versus placebo over weeks 5–28, corresponding to 0.26 attacks/month in the lonvo-z arm versus 2.10 with placebo. All key secondary endpoints were also met, including a 62% attack-free & therapy-free rate over the six-month evaluation period versus 11% for placebo. Safety looked clean in the initial topline dataset: all TEAEs were mild or moderate, no serious adverse events were reported in the lonvo-z arm, & the most common TEAEs were infusion-related reactions, headache, & fatigue. Intellia initiated a rolling BLA & expects to complete the submission in H2 2026, supporting a potential U.S. launch in H1 2027 if approved; additional HAELO data are expected at EAACI in June.

  - Mechanistically, lonvo-z uses lipid nanoparticle-delivered CRISPR/Cas9 to inactivate KLKB1, the hepatic gene encoding prekallikrein, with the goal of durably lowering kallikrein & downstream bradykinin production. This is mechanistically related to the validated kallikrein-inhibition approach used by chronic prophylactic therapies but differs by targeting the genomic source of prekallikrein rather than requiring continuous treatment. In HAE, dysregulated kallikrein-kinin signaling drives excess bradykinin, which increases vascular permeability & produces the recurrent swelling attacks that can involve the skin, abdomen, extremities, face, & upper airway (Longhurst & coworkers as published in 2012 in *The Lancet*; Kaplan & coworkers as published in 2010 in the *Journal of Allergy & Clinical Immunology*).

  - The Phase III result is clinically meaningful, but the competitive & capital-markets read-through is mixed. The 87% attack-rate reduction 62% attack-free/therapy-free rate is clearly supportive of registration, particularly given the one-time dosing proposition, but six-month efficacy data do not obviously surpass the most intensive established prophylaxis regimens. In the Phase III HELP study of lanadelumab, a kallikrein-targeting monoclonal antibody marketed by Takeda (4502-JP, NR), the 300 mg Q2W regimen reduced mean monthly attacks by 87% versus placebo, with monthly attack rates of 0.26 versus 1.97 over 26 weeks, & a post-hoc steady-state analysis reported 77% of patients attack-free during the final 16 weeks (Banerji & coworkers, published in 2018 in the *Journal of the American Medical Association*).

  - Cross-trial comparisons remain imperfect but are still useful to glean insights into drug effectiveness. 71% of HAELO patients entered on long-term prophylaxis & washed off prophylaxis before dosing, while HAELO's efficacy window began at week 5 to allow time for gene editing & kallikrein reduction to translate clinically. Longer follow-up is also important, as pooled Phase 1/2 data for the 50 mg dose showed a 96% mean attack-rate reduction & 31/32 patients attack-free & LTP-free with follow-up ranging from two months to three years, although that was an uncontrolled early-

stage dataset (Cohn & coworkers as published last year in the *New England Journal of Medicine* & separately by Magerl & coworkers in a poster presented earlier this year at the annual *American Academy of Allergy, Asthma & Immunology [AAAAI]* meeting). Some same-week HAE financing & M&A news adds to the debate: later in the week, April 29, Chiesi (private) agreed to acquire KalVista (KALV-Q, NR) for ~$1.9B, or $27/share in cash, adding EKTERLY/sebetralstat, an oral on-demand HAE therapy, while NTLA priced 16.7M shares at a discounted $10.75 to raise ~$180M gross despite the positive pivotal data & a rolling BLA path. This contrast evidence of durability, differentiation, & adoption for one-time in vivo editing.

- We continue to pay attention to clinical & regulatory developments in gene editing, particularly where they inform the broader modality debate across our coverage universe. The NTLA/KalVista contrast is a useful reminder that clinical elegance & commercial adoption are not the same question, especially when one-time genetic medicines are being evaluated against simpler chronic or episodic treatment models. In that context, the read-through to Satellos Bioscience (MSCL-T, Spec Buy, PT US$16.00) is indirect but useful. NTLA's hereditary angioedema results add to the broader investor conversation around one-time genetic medicines versus chronic or repeat-use disease-modifying therapies.

- That debate has relevance in Duchenne muscular dystrophy, where Satellos' SAT-3247 is positioned differently from genetic approaches as an oral, dystrophin-independent & mutation-agnostic small molecule intended to restore muscle repair & regeneration by targeting AAK1-mediated muscle stem-cell signalling. Precision BioSciences (DTIL-Q, NR) provides the closer DMD gene-editing analogue, with PBGENE-DMD designed as a one-time ARCUS-mediated excision therapy for patients with mutations between exons 45–55, a subgroup that could represent up to 60% of boys with Duchenne muscular dystrophy. The NTLA readout is directionally supportive for confidence in in vivo editing as a modality, but the financing/M&A contrast reinforces that one-time treatment is not automatically commercially dominant. Durability, safety, functional benefit, eligible population breadth, treatment burden, & patient/physician comfort with irreversible intervention remain central. For Satellos, BASECAMP pediatric Phase II data remain the key event to watch in Q4/26.

- **Oruka Therapeutics (ORKA-Q, NR) delivers competitive Phase IIa psoriasis data & prices an upsized US$700M equity offering; positive signal for extended-durability therapies, including Eupraxia's EP104GI.** ORKA-001, a half-life-extended IL-23p19 mAb, generated 63.5% PASI (Psoriasis Area & Severity Index) 100 (40/63) & 82.5% PASI 90 at Week 16 in EVERLAST-A, a randomized, double-blind, placebo-controlled Phase IIa trial in moderate-to-severe plaque psoriasis (n=84; 3:1 randomization; 600mg at Weeks 0 & 4; 26 sites across the US & Canada).

  - IGA 0 (Investigator's Global Assessment score of 0) mirrored PASI 100 at 63.5%, while IGA 0/1 reached 84.1%; all response rates used non-responder imputation. Safety was clean, with no serious TEAEs in the active arm, one severe TEAE in the placebo group, comparable overall TEAE rates (50.8% vs. 57.1%), no discontinuations due to AEs, & no injection-site reactions. Updated Phase 1 PK/PD data continue to support potential annual dosing, with ORKA-001 concentrations remaining above effective trough levels through 52 weeks after a single 600mg dose & no observed impact of anti-drug antibodies on PK in either Phase 1 or EVERLAST-A. Longer-term EVERLAST-A data, including Week 28 efficacy for all patients & 52-week follow-up for a subset, are expected in 2H26, while the dose-ranging Phase IIb EVERLAST-B trial is enrolling with data expected in 2027. Oruka rapidly monetized the readout, pricing an upsized US$700.4M public offering of 9.66M shares at US$72.50/share on April 28; the offering also includes a 30-day option for an additional 1.449M shares.

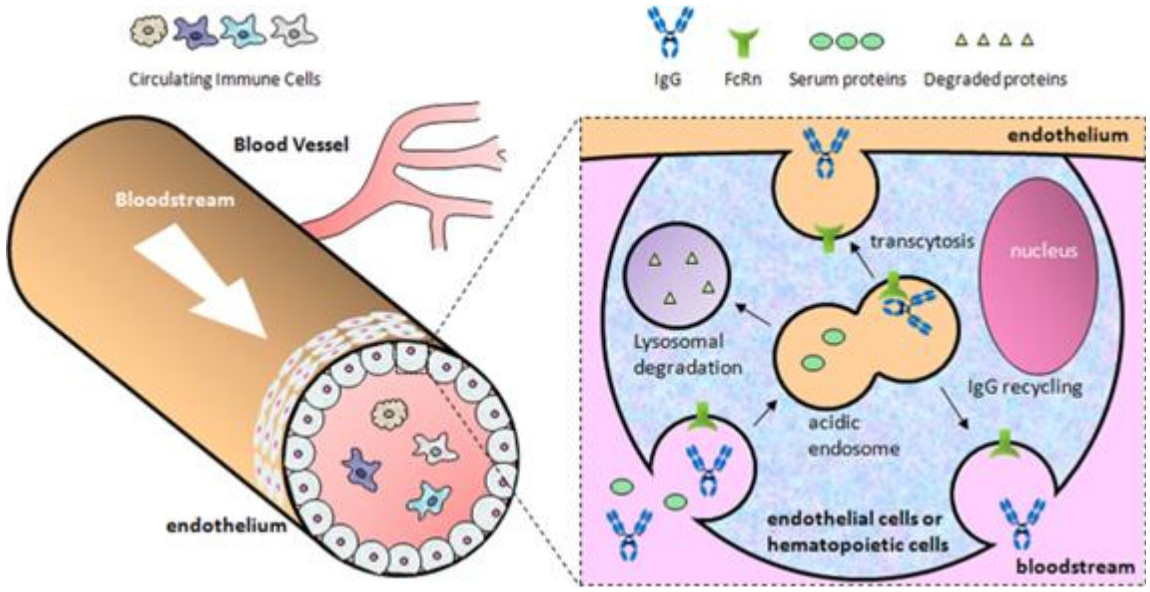
  - The clinical readout is strong, but the debate centers less on whether IL-23 inhibition works than on how much value accrues to convenience-led differentiation in a psoriasis market already served by highly effective biologics. The IL-23/Th17 axis is a well-validated driver of plaque psoriasis, & IL-23p19 agents such as risankizumab (Skyrizi) & guselkumab (Tremfya) have established the class as a dominant standard for high-efficacy biologic therapy (as described in two papers we reviewed, one published by Di Cesare & coworkers in 2009 in the *Journal of Investigative Dermatology* & the other published by Gordon & coworkers in 2018 in *The Lancet*). ORKA-001 is, consequently, a duration/exposure/dosing-burden story rather than a novel-mechanism pitch.

  - The relevant question is whether annual or twice-yearly dosing, if confirmed with durable PASI 90/100 maintenance, supports premium valuation & eventual commercial displacement versus quarterly Skyrizi or other high-clearance competitors. The financing is directionally positive for the extended-durability theme, even as the bar for differentiation rises. There is clearly investor appetite for long-duration versions of validated biology when efficacy is competitive, the

safety profile is familiar, & the commercial category is large. Another candidate we've mentioned in previous weeklies, Spyre's (SYRE-Q, NR) SPY001, fits the same pattern. Though we would keep the comparison secondary: open-label SKYLINE Part A UC data showed a 9.2-point RHI reduction at Week 12, 40% clinical remission, & 51% endoscopic improvement also reinforced interest in extended half-life biologics layered onto proven mechanisms.

- Mechanistically, ORKA-001 & SPY001 reflect a broader push to extend antibody durability through Fc engineering rather than new target biology. FcRn normally rescues internalized IgG from lysosomal degradation in acidified endosomes & recycles it back to circulation after dissociation at neutral pH. ORKA-001's YTE substitutions (M252Y/S254T/T256E) are designed to strengthen that pH-dependent FcRn interaction, increasing antibody recycling & systemic persistence while leaving IL-23p19 binding unchanged. SPY001 applies the same general principle to a validated IBD mechanism.

Exhibit 16. FcRn-Mediated IgG Recycling Supports Extended mAb Half-Life & Thus Extended Duration Of Benefit



Source: *Experimental & Molecular Medicine (2019). Vol. 51, pp. 138-147*

- We view these developments as confirmatory/constructive for Eupraxia (EPRX-Q, Buy, PT US$12.75), where EP-104GI offers even more than the convenience argument (though annual dosing still is a large aspect of their differentiation). In EoE, Eupraxia is not stretching an established systemic biologic into less frequent dosing. EP-104GI is designed to deliver fluticasone locally into diseased esophageal tissue through DiffuSphere, with the goal of improving duration while limiting systemic steroid exposure. RESOLVE Cohort 9 (n=3, 20x8mg dose) showed 90% & 88% reductions in EoEHSS stage & grade at Week 36, a 72% peak eosinophil count reduction, a 3-point mean SDI improvement, & 66% clinical remission maintained from Week 8 through Week 36 after a single administration. Safety remains clean across 31 treated patients & >230 patient-months of follow-up, with no drug-related SAEs, no oropharyngeal candidiasis, & no adrenal insufficiency or glucose derangement.

- **AbbVie secures option to acquire Kestrel Therapeutics (private), adding early exposure to oral pan-Kras inhibition**. IL-based AbbVie (ABBV-NY, NR) entered into a warrant-based strategic agreement with privately held Kestrel Therapeutics that gives AbbVie an exclusive option to acquire the company if defined development & regulatory milestones are met. The total potential deal value, including upfront, option exercise payments & downstream milestones, could reach US$1.45B.

  - The agreement is centered on KST-6051, Kestrel's investigational oral pan-Kras inhibitor, which dosed its first patient this week in the Phase I FALCON study in Kras-mutant advanced or metastatic solid tumors. KST-6051 is designed to bind Kras in both active/GTP-bound & inactive/GDP-bound states while selectively sparing HRAS/NRAS, with planned development across PDAC, CRC, NSCLC & other Kras-driven malignancies. Kestrel's pan-Kras approach joins a crowded wave of direct Kras inhibition programs; EU-based AstraZeneca (AZN-LN, NR) licensed Jacobio's pan-Kras

inhibitor JAB-23E73 in Dec/25 in a deal valued at up to US$2B, & we covered Revolution Medicines' (RVMD-Q, NR) positive Phase III RASolute 302 readout for daraxonrasib in 2L metastatic PDAC two weeks ago (13.2- vs. 6.7-month median OS; HR 0.40, p<0.0001). AbbVie itself was the subject of RVMD acquisition speculation earlier this year before publicly denying those reports; the Kestrel option certainly represents a more measured entry into RAS-directed oncology at a substantially lower upfront commitment.

- For our coverage universe, the most relevant read-through is to Oncolytics Biotech (ONCY-Q, Spec Buy, PT US$3.00), not because pelareorep is a direct Kras inhibitor, but because the same Ras-activated tumor biology is central to the firm's colorectal cancer strategy. In some of the foundational reovirus literature, it was found to preferentially replicate in cells with constitutively activated Ras signaling, an observation that provided the foundational rationale for evaluating reovirus-based therapy in Ras-driven tumors (as originally characterized in the 1998 *Science* paper to which we referred in our Oncolytics commentary above & which supported the company's founding that year). Oncolytics is developing pelareorep, an IV-administered oncolytic reovirus, in Kras-mutant MSS metastatic colorectal cancer, where the drug is intended to exploit activated Ras biology to drive selective viral oncolysis & downstream immune activation rather than directly inhibit Kras itself.

- While Kras inhibition has reached modest late-stage validation in CRC, activity has been confined to the Kras G12C subtype in chemo-refractory settings (sotorasib + panitumumab: 5.6-month median PFS, 26.4% ORR in 3L+ Kras G12C mCRC; Fakih & coworkers as published in 2023 in the *New England Journal of Medicine*), leaving the broader RAS-mutant MSS population largely unaddressed by small-molecule approaches alone. Kras-mutant MSS tumors are also critically defined by their resistance to checkpoint immunotherapy, durable disease control in this population will likely require strategies that combine pathway inhibition with immune activation rather than rely on either scenario in isolation.

- That logic favors pelareorep's mechanism, which is designed to convert activated Ras signaling into an immunogenic vulnerability rather than simply suppress it. Pelareorep + bevacizumab/FOLFIRI received FDA Fast Track designation in 2L Kras-mutant MSS mCRC in February 2026, supported by Phase I REO 022 data reporting 33% ORR, 16.6-month median PFS & 27-month median OS, though against historical benchmarks rather than a randomized control arm. The randomized Phase II REO 033 study, now enrolling, compares bevacizumab/FOLFIRI with or without pelareorep in 2L RAS-mutated MSS mCRC (~30 patients per arm, ORR primary endpoint, interim data expected by year-end).

- Compass Therapeutics misses survival endpoint as a second-line therapy for biliary tract cancer. MA-based Compass Therapeutics (CMPX-Q, NR) reported key secondary endpoints from the randomized Phase II/III COMPANION-002 trial evaluating tovecimig (DLL4 x VEGF-A bispecific antibody) plus paclitaxel versus paclitaxel alone in 168 patients with second-line advanced biliary tract cancer (BTC), randomized 2:1. Tovecimig met the PFS secondary endpoint, delivering a median PFS of 4.7 months versus 2.6 months (HR=0.44, p<0.0001). However, the OS secondary endpoint did not reach statistical significance: median OS was 8.9 months in the tovecimig arm versus 9.4 months for the control arm (HR=1.05, p=0.78), confounded by a 54% crossover rate from the control arm. The previously reported primary endpoint of ORR was 17.1% versus 5.3% (p=0.031).

- The company highlighted a post-hoc subset analysis showing crossover patients survived longer than non-crossover patients in the control arm (12.8 vs. 6.1 months, HR=0.54, p=0.04), but this comparison is subject to immortal time bias: crossover patients had to survive long enough after progression to remain eligible & actually receive tovecimig, banking survival time that non-crossover patients, many of whom likely deteriorated too rapidly to receive additional therapy, did not have the opportunity to accrue. Also, a pre-specified RPSFT (rank-preserving structural failure time) analysis, statistical method designed to adjust for exactly this type of crossover contamination, also failed to demonstrate an OS benefit (HR=1.13, p=0.65). Compass acknowledged the model's key assumptions were not met in this dataset, but the failure of the pre-specified adjustment alongside reliance on post-hoc descriptive comparisons weakens the case that crossover alone explains the OS miss. Compass still intends to meet with the FDA in advance of a planned BLA submission. Safety was consistent with prior reports, with hypertension (69%) & fatigue (67%) the most common TEAEs in the combination arm; Grade 3+ events included hypertension (44%) & neutropenia (36%).

  - Tovecimig simultaneously blocks DLL4 (Delta-like ligand 4, a Notch pathway ligand) & VEGF-A, two key mediators of tumor angiogenesis. Dual inhibition is intended to overcome the compensatory upregulation of Notch signaling that occurs with VEGF blockade alone, a resistance mechanism well-characterized in preclinical models (Noguera-Troise & coworkers as published in 2006 in the journal *Nature*, also as published by Ridgway & coworkers in the same

year/journal). DLL4/Notch inhibition promotes non-productive, disorganized angiogenesis that impairs tumor perfusion, while VEGF-A blockade reduces vascular permeability & new vessel formation. The combination with paclitaxel provides a cytotoxic backbone in a second-line setting where there is no FDA-approved standard of care for BTC patients without actionable mutations. The biological rationale for anti-angiogenic therapy in BTC is less established than in hepatocellular carcinoma, where tumor hypervascularity underpins the efficacy of bevacizumab-based regimens as part of frontline standard of care with PD-1/PD-L1 inhibition (Finn & coworkers, published in 2020 in the *New England Journal of Medicine*); biliary tract tumors are generally less vascularized, which may temper expectations for the magnitude of benefit from VEGF-targeted approaches in this histology.

- This data would have been on the radar for Montreal-based Knight Therapeutics (GUD-T, NR), which holds Latin American rights to Incyte's pemigatinib (Pemazyre) for FGFR2-altered cholangiocarcinoma. Knight sits on the opposite side of the BTC treatment paradigm: a molecularly targeted agent in a genetically defined subset versus tovecimig's mutation-agnostic anti-angiogenic approach in unselected patients. The difficulty translating PFS into OS in the broader population is a reminder of why the field has moved towards personalized medicine via biomarker selection in this disease, & a tovecimig approval for FGFR-negative patients would expand the second-line landscape rather than encroach on pemigatinib's niche.

- **One of ProMIS' Alzheimer's disease drug development peers fails in Phase II clinical testing.** CA-based CNS drug developer Alector (ALEC-Q, NR) reported this week that its 367-patient Phase II Alzheimer's disease trial (the PROGRESS-AD trial) that was testing the firm's sortilin receptor-targeted mAb AL101/nivisnebart did not meet expectations on impacting disease progression (the primary endpoints were multiple, but included impact on the Clinical Dementia Rating-Sum of Boxes cognition scale & on the Alzheimer's Disease Rating Scale at one-year follow-up).

  - Alector was one of the peer firms for MA-based ProMIS Neurosciences (PMN-Q, Spec Buy, PT US$46.00) that we identified in our original report & on that basis is a firm that we tracked for assessing advanced in the Alzheimer's disease clinical landscape, a landscape that was revised substantially in recent years through the FDA approval of Eisai's (4523-JP, NR) lecanemab/Leqembi & Eli Lilly's (LLY-NY, NR) donanemab/Kisunla & even Biogen's (BIIB-Q, NR) aducanumab/Adehelm, though Biogen returned aducanumab rights to private Switzerland-based innovator Neurimmune in 2024.

  - Alector was partnered with UK-based pharma giant GlaxoSmithKline (GSK-LN, NR) on AL101/nivisnebart development & indeed the anti-sortilin receptor mAb was identified as GSK4527226 in Glaxo's own CNS clinical pipeline. The trial was discontinued based on an interim futility analysis that thus indicates that AL101/nivisnebart's mechanism of action – by down-regulating the sortilin receptor (sortilin is a highly-expressed intracellular protein in the central nervous system that normally functions as an intracellular transporter of other proteins within neurons, getting them where they need to go in order to confer their normal cellular functions), it was thought that levels of the neuron function-supporting protein progranulin could be elevated & impact cognition in the process. Progranulin's physiology may still be relevant to Alzheimer's disease progression & cognitive impairment, but it appears not to be independently relevant to cognition, at least not in this trial & not as impacted by AL101/nivisnebart on its own.

  - Alector's Alzheimer's disease clinical program does not bear significantly on ProMIS' own PRECISE-AD trial, for which the firm is testing its beta-amyloid oligomer-targeted mAb PMN310 in a similarly-designed but smaller Phase II Alzheimer's disease program. The 144-patient trial was fully-enrolled in Dec/25 (& it is designated in the US NIH's clinical database as active, not recruiting) & thus is on pace to report interim six-month cognition & biomarker data later this quarter & then report final one-year cognition & biomarker data by end-of-FQ426, with slippage on timelines into the subsequent quarter a reasonable expectation in our view & in our model.

  - It is at this point that we infuse a bit of candor into our expectations for PMN310 performance in PRECISE-AD – the trial is in our view too small & too brief to observe measurable impact on cognition at a six-month endpoint, even before considering that a one-year follow-up on 144 Alzheimer's disease patients may itself be at the limits of observable cognition impact – Eisai's pivotal Phase III CLARITY-AD trial was far larger & far longer duration (1795 patients, assessed at 18-month follow-up) as was Eli Lilly's Phase III TRAILBLAZER-ALZ 2 trial (1736 patients, also 18-month follow-up). But what we will be closely monitoring will be impact on CNS biomarkers (specifically levels of PET-confirmed beta-amyloid plaques in the brain & levels of phosphorylated tau protein in cerebrospinal fluid – mainly pTau 181 & pTau 217, as readily quantifiably by already-FDA-approved Elecsys pTau assays developed by Roche [ROG-SW, NR], for example) that have been shown to be early predictors of future cognitive impact, as ProMIS itself reported as being relevant to

Alzheimer's disease progression in a Nov/25 *Alzheimer's & Dementia* study (published independently from a distinct PMN310 study that ProMIS published in the same journal; see below). We would consider any biomarker shifts that are well-documented to be predictive of future cognitive improvement to be positive to our PMN investment thesis & on the role of beta-amyloid oligomers in cognitive impairment.

- **Summary & valuation.** Our PT/rating on PMN is unchanged by a competitor's Phase II update that by being negative for the relevant drug & its mechanism of action does not in any way impact our PMN investment thesis that rests squarely on our medical diligence on the role of beta-amyloid oligomers on Alzheimer's disease etiology.
  - All published data on PMN310 shows us that the mAb is more oligomer-selective in its beta-amyloid binding than peer drugs, excluding perhaps Acumen's (ABOS-Q, NR) ACU193/sabirnetub that was also designed to be oligomer-selective, & with minimal competitive binding to beta-amyloid monomers or plaques that can lead to antibody binding in the brain, leading to localized brain swelling (so-called ARIA-E) episodes in the process. This characteristic is well-documented in the medical literature, including but not limited to a Nov/25 study published by ProMIS' scientific team in the journal *Alzheimer's & Dementia*. Our PT is based on NPV (30% discount rate) & multiples of our F2032 EBITDA/fd EPS forecasts of US$199.7M & US$7.40/shr, respectively.
  - Though our attention is squarely focused on PMN310 & on pending PRECISE-AD milestones, our model does ascribe value to secondary mAbs in ProMIS pipeline that target other CNS-relevant misfolded proteins, including misfolded alpha-synuclein in Parkinson's disease with PMN442 & misfolded TDP-43 in amyotrophic lateral sclerosis with PMN267, both of which were generated using Neil Cashman's (ProMIS' Chief Scientific Officer) techniques for synthesizing cyclic peptides that mimic disease-relevant conformational epitopes in misfolded protein diseases. IND-enabling studies are assumed to be ongoing & to support commencement of initial Phase I studies for both mAbs sometime in F2027.

Exhibit 17. ProMIS' Clinical Pipeline Of Conformational Epitope-Targeted CNS-Disease-Focused mAbs, Led By PMN310

Asset	Target protein	Disease indication	Normal physiological role	Stage	Timelines to next milestone
				Discovery / Preclinical / I / II / III	
Lead antibodies in formal preclinical/IND-enabling testing					
PMN310	Epitope exposed in beta-amyloid oligomers	Alzheimer's disease	Synaptic plasticity, memory formation in hippocampus	II	Phase I completed, data in FH224 PRECISE-AD is active; data in FH226
PMN267	TDP-43 (Transactive response DNA-bind protein)	Amyotrophic lateral sclerosis (ALS)	Transcription factor (mRNA homeoasis/processing)	Preclinical	Complete IND-enabling studies, FH126 Commence Phase I ALS trial, FQ127
PMN442	Alpha-synuclein (pre-synaptic tetramer in the brain)	Parkinson's disease, multiple system atrophy	Controls neurotransmitter release, vesicle transport	Preclinical	Complete IND-enabling studies, FH126 Commence Phase I PD/MSA trial, FQ127
Misfolded protein antigens being targeted in discovery					
TBD	RACK1, SOD1	Amyotrophic lateral sclerosis (ALS)	Protein synthesis	Discovery	Lead mAb generation by FH226-FH127
TBD	Tau	Alzheimer's disease Frontotemporal lobar degeneration (FTLD)	Microtubule stabilization neuron generation	Discovery	Lead mAb generation by FH226-FH127
TBD	DISC1	Schizophrenia	Neuron generation mitochondrial transport	Discovery	Lead mAb generation by FH226-FH127
TBD	Beta-amyloid vaccine	Alzheimer's disease prevention	Synaptic plasticity, memory formation in hippocampus	Discovery	Lead mAb generation by FH226-FH127

Source: ProMIS Neurosciences financial filings, Leede Financial

Capital Markets Summary

Exhibit 18. EBITDA Or EPS-Positive Canadian Healthcare Stocks

Company	Filing Curr.	Sym.	Shrs Out. (M)	Share Price 30-Apr	Mkt Cap (M)	Mkt Cap (C$M)	Ent. Value (M)	Ent. Value (C$M)	EV/EBITDA (T12M)	EV/EBITDA FY1	EV/EBITDA FY2	Price/Earnings (T12M)	Price/Earnings FY1	Price/Earnings FY2
Profitable Canadian healthcare firms - specialty services [2,4]														
DRI Healthcare Trust	CAD	DHT.UN	55.0	$16.45	905	905	1,508	1,508	7.2x	6.9x	6.6x	NA	7.3x	7.2x
Jamieson Wellness	CAD	JWEL	41.5	$33.13	1,374	1,374	1,823	1,823	11.6x	10.2x	9.2x	22.2x	15.6x	13.4x
K-Bro Linen	CAD	KBL	13.0	$37.75	490	490	787	787	7.6x	7.2x	6.8x	25.5x	18.4x	15.1x
Medical Facilities [1]	CAD	DR	17.6	$12.46	219	299	409	559	6.5x	7.1x	7.1x	21.9x	6.1x	18.6x
Microbix Biosystems	CAD	MBX	138.0	$0.25	35	35	32	32	NA	NA	11.1x	NA	NA	NA
Savaria	CAD	SIS	71.9	$29.79	2,141	2,141	2,329	2,329	12.8x	11.4x	10.4x	31.0x	21.5x	19.0x
Profitable Canadian healthcare firms - specialty pharmaceuticals development/sales [2]														
Aurinia Pharma	USD	AUPH	129.9	$15.28	1,985	2,717	1,656	2,267	9.6x	7.5x	6.3x	7.1x	19.3x	14.6x
Bausch Health	USD	BHC	373.5	$5.59	2,088	2,857	30,876	42,251	6.6x	5.8x	6.0x	13.2x	1.3x	1.3x
BioSyent	CAD	RX	11.6	$14.61	170	170	142	142	11.7x	9.2x	7.8x	18.3x	15.5x	13.0x
Cipher Pharma [1]	CAD	CPH	25.4	$13.23	336	460	457	625	18.9x	16.1x	12.9x	12.3x	17.8x	13.9x
HLS Therapeutics [1]	CAD	HLS	31.3	$3.43	107	147	199	272	12.1x	9.8x	8.3x	NA	NA	NA
Knight Therapeutics	CAD	GUD	98.3	$7.45	732	732	696	696	10.3x	9.2x	8.6x	NA	45.8x	29.4x
Medexus Pharma [1]	CAD	MDP	32.0	$2.89	93	127	141	193	10.3x	8.8x	6.4x	NA	NA	9.0x
Profitable Canadian healthcare firms - eldercare services or infrastructure developers														
CareRx	CAD	CRRX	62.9	$3.64	229	229	293	293	9.7x	7.9x	7.0x	8.8x	21.8x	11.9x
Chartwell Retirement	CAD	CSH.UN	324.0	$21.22	6,875	6,875	9,754	9,754	24.3x	19.3x	17.6x	NA	NA	55.8x
Extendicare	CAD	EXE	94.8	$30.19	2,863	2,863	2,845	2,845	16.2x	12.1x	10.7x	26.7x	24.8x	21.2x
Vital Infrastructure	CAD	VITL.UN	250.0	$5.54	1,385	1,385	2,661	2,661	10.3x	12.4x	12.6x	NA	NA	NA
Nova Leap Health	CAD	NLH	87.3	$0.37	32	32	34	34	12.9x	NA	NA	NA	NA	NA
Sienna Senior Living	CAD	SIA	106.0	$23.37	2,478	2,478	3,784	3,784	25.2x	18.9x	17.1x	47.7x	39.0x	33.9x
Profitable Canadian healthcare firms - medical equipment distribution/sales [3]														
Covalon Technologies	CAD	COV	27.6	$1.85	51	51	35	35	24.5x	10.2x	6.6x	51.9x	26.4x	13.2x
Viemed Healthcare	USD	VMD	38.5	$9.89	381	381	522	714	7.7x	5.7x	5.0x	25.6x	20.6x	16.0x
Profitable Canadian healthcare firms - healthcare IT or digital IT services firms														
Healwell AI	CAD	AIDX	295.6	$0.93	275	275	342	342	NA	41.3x	21.0x	NA	NA	NA
Hydreight	CAD	NURS	53.4	$4.09	218	218	208	208	NA	9.1x	7.5x	NA	13.6x	8.3x
Kneat.com	CAD	KSI	96.1	$4.44	427	584	407	407	NA	23.4x	15.8x	NA	NA	NA
Vitalhub	CAD	VHI	63.3	$8.10	512	701	396	396	17.4x	11.6x	9.7x	NA	32.1x	25.7x
Well Health	CAD	WELL	255.5	$4.21	1,076	1,076	1,829	1,829	9.1x	10.2x	9.3x	NA	15.1x	11.0x
Average									**12.8x**	**12.1x**	**9.9x**	**24.0x**	**20.1x**	**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***
Dentalcorp Holdings	***CAD***	***DNTL***	***192.0***	***$11.00***	***2,112***	***2,112***	***3,112***	***3,112***	***10.9x***	***NA***	***NA***	***NA***	***NA***	***NA***
Quipt Home Medical	***USD***	***QIPT***	***44.5***	***$3.65***	***162***	***223***	***235***	***323***	***5.4x***	***NA***	***NA***	***2.1x***	***NA***	***NA***
Theratechnologies	***CAD***	***TH***	***46.0***	***$4.47***	***206***	***206***	***238***	***238***	***12.3x***	***NA***	***NA***	***NA***	***NA***	***NA***

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

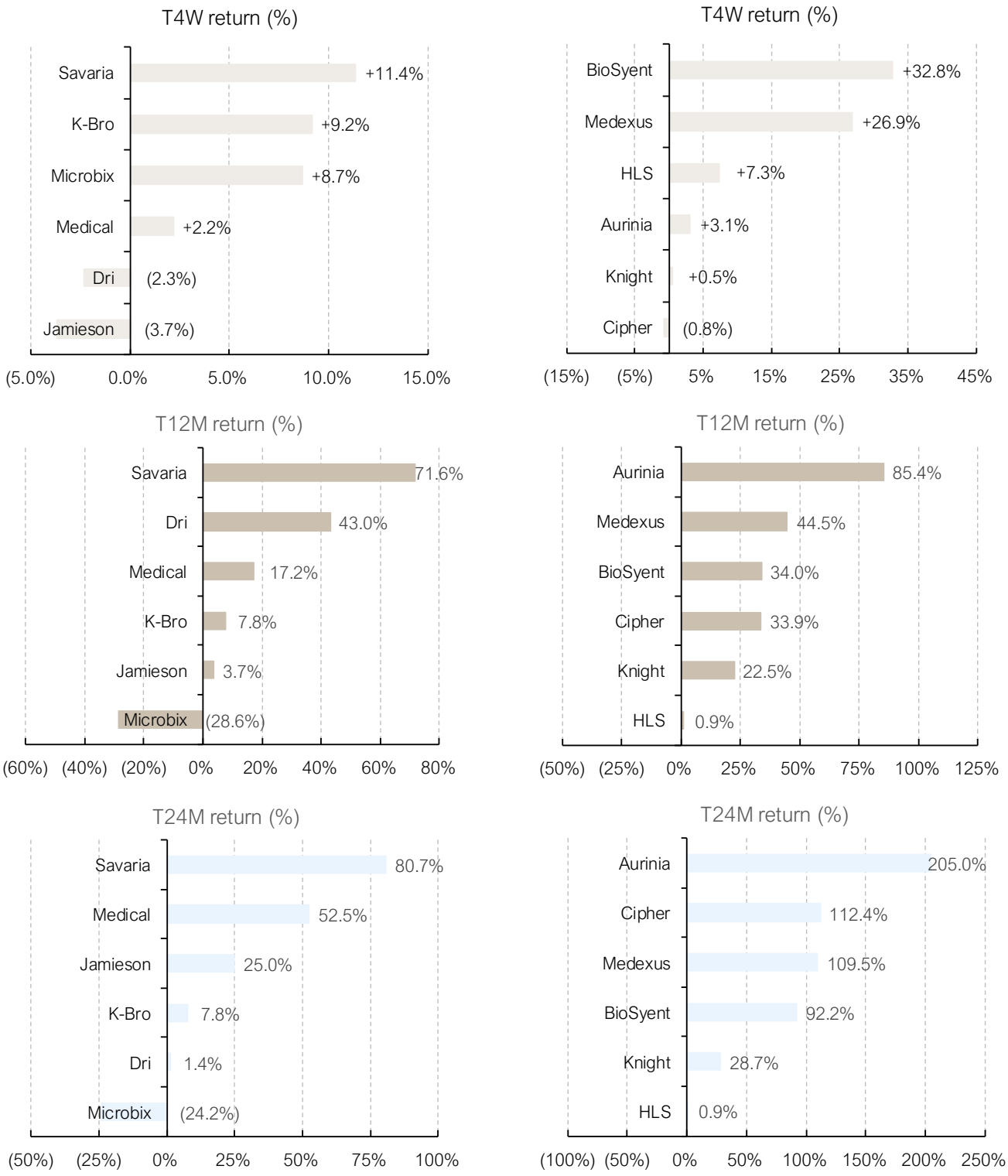
[2] Legacy specialty pharmaceutical firm & coverage stock Theratechnologies (TH-T, THTX-Q) was acquired in Sept/25 by CB Biotechnology/Future Pak for cumulative consideration of US$4.20/shr; Andlauer's acquisition by UPS (UPS-NY, NR) is closed as of Nov/25

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

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

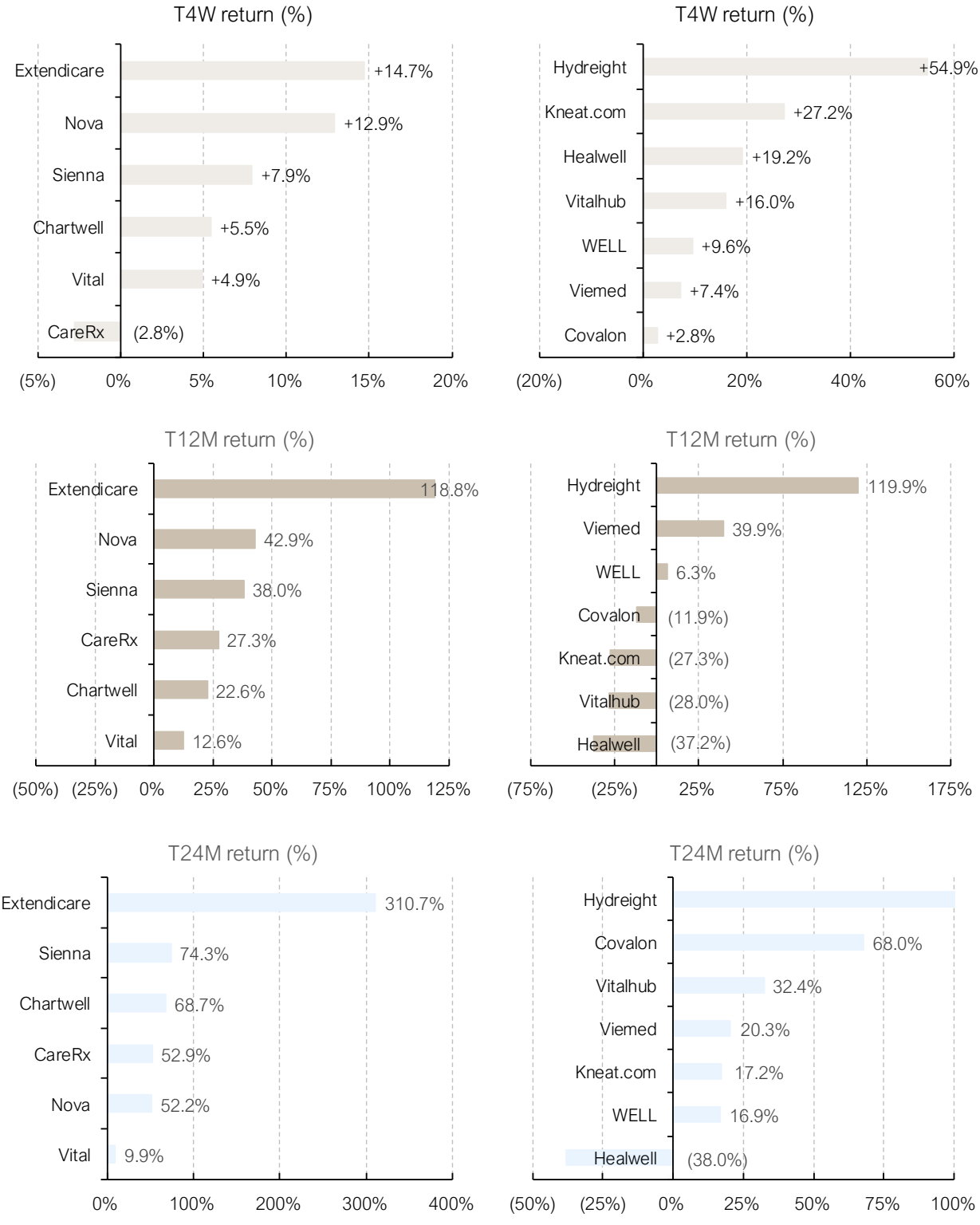
Source: Refinitiv, company reports, Leede Financial

Exhibit 19. 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 20. 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 1,473%)*

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Speculative Buy	The security is considered a BUY but carries an above-average level of risk.
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RECOMMENDATION	NO. OF COMPANIES	%
Buy	9	60%
Speculative Buy	4	26%
Hold	1	7%
Sell	-	-
Tender	-	-
Under Review	1	7%

Historical Target Price

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