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CRDL-TSX, CRDL-NASDAQ

Rating:	Speculative Buy
Target:	C\$7.00 (was C\$11.00)
Price:	\$1.29
Return:	443%
Valuation:	NPV, 20x EPS, 12.5x EV/EBITDA (F2031 estimates, 25% disc)

Market Data

Basic Shares O/S (M)	94.0
FD Shares O/S (M)	106.9
Market capitalization (\$M)	121.3
Enterprise Value (\$M)	93.7
Pro forma cash (\$M, Inc Oct/24 offer)	27.6
LT debt (\$M, most rec Q)	0.0
52 Week Range	\$1.09-\$2.30
Avg. Weekly Volume (000)	635,675
Fiscal Year End	31-Dec

Key Milestones (Calendar Year)

CardiolRx, PhII pericarditis data (pilot-MAVERIC), Jun/24	Q224
CardiolRx, commence Phase II/III pericarditis trial (MAVERIC), Apr/25	Q125
CardiolRx, PhII myocarditis data (ARCHER), Aug/25 & Dec/25	Q325, Q425
CRD-38, IND filing for heart failure with preserved ejection fraction (HFpEF)	H126

Financial Metrics

In C\$000	2029E	2030E	2031E
Rev, acute myocarditis	\$0	\$0	\$33,573
Rev, recur pericarditis	\$32,597	\$81,981	\$107,214
Rev, HFpEF	\$0	\$0	\$42,954
Total Revenue (\$000)	\$32,597	\$81,981	\$183,742
EBITDA (\$000)	\$10,812	\$58,757	\$157,993
Adj net inc (\$000)	\$6,796	\$40,358	\$109,823
EPS (basic)	\$0.07	\$0.43	\$1.17
EPS (FD)	\$0.06	\$0.38	\$1.03

Company Description

Cardiol Therapeutics is an ON-based cardiovascular disease drug developer, focused on its Phase II/III-stage oral cannabidiol formulation CardiolRx & injectable cannabidiol form CRD-38 in inflammatory heart diseases, including recurrent pericarditis, acute myocarditis, & diastolic heart failure.



Source: Refinitiv, Leede Financial

ARCHER Update. Clear Efficacy Signals In CardiolRx-Treated Myocarditis Patients, If Not Quite To Statistical Significance On A Few Measures – Spec Buy

ON-based small-molecule cardiovascular disease drug developer Cardiol Therapeutics reported more comprehensive efficacy data from its 109-patient Phase II acute myocarditis study (the ARCHER trial) at a cardiovascular disease-focused medical conference in Italy over the weekend. Recall that ARCHER was testing Cardiol's lead cardiovascular disease-targeted anti-inflammatory orally-active ultra-pure synthetic cannabidiol formulation CardiolRx for the indication. Patient enrollment for the twelve-week trial concluded in late FQ324 & a preliminary fairly qualitative description of ARCHER data were initially provided in mid-FQ325, on which we provided some correspondingly qualitative commentary at the time.

Bottom line. Capital markets responded negatively to Cardiol's ARCHER trial update & as our commentary below will describe, we too were cautious on commentary shared yesterday, though we suspect that our caution is not for the same reason as broader capital markets caution. As a guess, we believe that most CRDL followers reflexively assumed that because ARCHER's co-primary endpoints (impact on cardiac MR-assessed change in extracellular volume & on global longitudinal strain, both measures of structural heart disease & cardiac function) were indeed missed on statistical merits – which we already knew from Cardiol's preliminary update shared in Aug/25 – this implies that CardiolRx was ineffective in this indication & that data reflects negatively on the drug's more general anti-inflammatory activity in other targeted cardiovascular indications. On this we disagree with capital markets sentiment, if we are interpreting that sentiment correctly.

Our perspective on ARCHER commentary (as distinct from ARCHER data themselves) is correspondingly cautious but for a different reason that is not directly influenced by lack of statistical significance on all ARCHER endpoints, endpoints for which all trends favored CardiolRx in what was a small Phase II trial by cardiovascular standards. We believe that Cardiol followers who are excessively focused on p-values that are close to, but slightly above, 0.05 are missing CardiolRx's clear clinical (though not statistical) significance in acute myocarditis that ARCHER data reveal

Cardiol provides no details on its go-forward strategy in acute myocarditis, leading us to assume for now that the indication is secondary to other ongoing cardiovascular programs. It was clear from Cardiol's conference call describing ARCHER data that the trial was more useful to Cardiol for the mechanistic foundations that it provides in support of other cardio-metabolic indications, mainly recurrent pericarditis & diastolic heart failure to which our model separately ascribes value. We agree with that perspective.

But what was separately embedded in Cardiol's commentary, or more precisely what was omitted from Cardiol's commentary, was any allusion to a go-forward Phase III acute myocarditis clinical strategy, an omission that suggests to us that Cardiol plans to defer any future myocarditis testing without actually saying so, probably until Phase III recurrent pericarditis data are available from the ongoing MAVERIC trial & until Phase I/II heart failure testing with injectable cannabidiol formulation CRD-38 is well-advanced.

Exhibit 1. CardiolRx (Acute Myocarditis/Recurrent Pericarditis) & CRD-38 (HFpEF) Royalty Revenue Forecasts For Cardiol

Year-end December 31 (C\$000, exc per share data)	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Acute Myocarditis, US										
Current Population, United States	342,130,165	344,182,946	346,248,043	348,325,532	350,415,485	352,517,978	354,633,086	356,760,884	358,901,449	361,054,858
Proportion, Acute myocarditis	75,269	75,720	76,175	76,632	77,091	77,554	78,019	78,487	78,958	79,432
Target Medical Population, adj for recovery cases	55,699	56,033	56,369	56,707	57,048	57,390	57,734	58,081	58,429	58,780
Price per treated patient (US\$)	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000	\$20,000
Est. value of target medical market (US\$000)	\$1,113,976	\$1,120,660	\$1,127,384	\$1,134,148	\$1,140,953	\$1,147,799	\$1,154,685	\$1,161,613	\$1,168,583	\$1,175,595
% Market Share	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	25.0%	30.0%	40.0%	50.0%
Gross revenue, CardiolRx (US\$000)	\$0	\$0	\$0	\$0	\$0	\$114,780	\$288,671	\$348,484	\$467,433	\$587,797
Gross revenue, CardiolRx (C\$000)	\$0	\$0	\$0	\$0	\$0	\$149,214	\$375,273	\$453,029	\$607,663	\$764,137
Less: Proportion of gross rev to Dalton/Purisys (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Gross revenue, CardiolRx (C\$000)	\$0	\$0	\$0	\$0	\$0	\$111,910	\$281,455	\$339,772	\$455,747	\$573,102
Royalty rate on net sales (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CardiolRx (Myocarditis), royalty rev (C\$000)	\$0	\$0	\$0	\$0	\$0	\$33,573	\$84,436	\$101,932	\$136,724	\$171,931
Recurrent Pericarditis, US										
Current Population, United States	342,130,165	344,182,946	346,248,043	348,325,532	350,415,485	352,517,978	354,633,086	356,760,884	358,901,449	361,054,858
Annual incidence, acute pericarditis	94,770	95,339	95,911	96,486	97,065	97,647	98,233	98,823	99,416	100,012
Proportion, recurrent pericarditis	31,274	31,462	31,651	31,840	32,031	32,224	32,417	32,612	32,807	33,004
Proportion, second-third-fourth recurrence	10,946	11,012	11,078	11,144	11,211	11,278	11,346	11,414	11,483	11,551
Price per treated patient (US\$)	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000	\$50,000
Est. value of target medical market (US\$000)	\$547,297	\$550,581	\$553,884	\$557,208	\$560,551	\$563,914	\$567,298	\$570,701	\$574,126	\$577,570
% Market Share	0.0%	0.0%	0.0%	20.0%	50.0%	65.0%	70.0%	75.0%	75.0%	75.0%
Gross revenue, CardiolRx (US\$000)	\$0	\$0	\$0	\$111,442	\$280,275	\$366,544	\$397,108	\$428,026	\$430,594	\$433,178
Gross revenue, CardiolRx (C\$000)	\$0	\$0	\$0	\$144,874	\$364,358	\$476,507	\$516,241	\$556,434	\$559,773	\$563,131
Less: Proportion of gross rev to Dalton/Purisys (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Gross revenue, CardiolRx (C\$000)	\$0	\$0	\$0	\$108,655	\$273,269	\$357,381	\$387,181	\$417,325	\$419,829	\$422,348
Royalty rate on net sales (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CardiolRx (Pericarditis), royalty rev (C\$000)	\$0	\$0	\$0	\$32,597	\$81,981	\$107,214	\$116,154	\$125,198	\$125,949	\$126,705
Diastolic Heart Failure, US										
Current Population, United States	342,130,165	344,182,946	346,248,043	348,325,532	350,415,485	352,517,978	354,633,086	356,760,884	358,901,449	361,054,858
Heart failure prevalence, all subcategories	6,737,538	6,777,963	6,818,631	6,859,543	6,900,700	6,942,104	6,983,757	7,025,660	7,067,814	7,110,220
Prevalence, diastolic heart failure (HFpEF)	3,368,769	3,388,982	3,409,316	3,429,772	3,450,350	3,471,052	3,491,879	3,512,830	3,533,907	3,555,110
Annual incidence, diastolic heart failure (HFpEF)	285,050	286,760	288,481	290,211	291,953	293,704	295,467	297,239	299,023	300,817
Price per annual course of therapy (US\$)	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000	\$5,000
Est. value of target medical market (US\$000)	\$1,425,248	\$1,433,800	\$1,442,403	\$1,451,057	\$1,459,764	\$1,468,522	\$1,477,333	\$1,486,197	\$1,495,114	\$1,504,085
% Market Share	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	20.0%	25.0%	30.0%	35.0%
Gross revenue, CRD-38 (US\$000)	\$0	\$0	\$0	\$0	\$0	\$146,852	\$295,467	\$371,549	\$448,534	\$526,430
Gross revenue, CRD-38 (C\$000)	\$0	\$0	\$0	\$0	\$0	\$190,908	\$384,107	\$483,014	\$583,095	\$684,359
Less: Proportion of gross rev to Dalton/Purisys (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Gross revenue, CRD-38 (C\$000)	\$0	\$0	\$0	\$0	\$0	\$143,181	\$288,080	\$362,261	\$437,321	\$513,269
Royalty rate on net sales (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CRD-38 (Diastolic HF), royalty rev (C\$000)	\$0	\$0	\$0	\$0	\$0	\$42,954	\$86,424	\$108,678	\$131,196	\$153,981
Total product royalty revenue (C\$000)	\$0	\$0	\$0	\$32,597	\$81,981	\$183,742	\$287,015	\$335,807	\$393,869	\$452,616

Source: Historic data – Cardiol financial filings; Forecasts/Estimates – Leede Financial Inc.

We understand the implied strategy on deploying capital toward other cardiovascular indications & not to acute myocarditis, but the reality from our perspective is that an indication to which our model ascribed value & still does is unlikely to conclude pivotal Phase III testing & FDA review over the timeline we previously projected & we are revising our model accordingly. Under best-case scenario, we now assume that pivotal Phase III acute myocarditis testing could commence after MAVERIC/recurrent pericarditis data are in the public domain, possibly later in FH226 or in early FH127.

ARCHER data were positive on balance in our view, notwithstanding capital markets response that clearly dissents from that opinion. We were encouraged by CardiolRx's impact on heart pathology in ARCHER for which we now have new quantification. For example, oral dosing of CardiolRx (at three-month follow-up in all cases) was associated with statistically-significant improvement in MR-confirmed left ventricular mass (LVM) as compared to placebo patients, with a p-value of 0.01, while a different measure of structural heart pathology called left atrial end-systolic volume (LAESV; the volume of the left atrium after it empties oxygenated blood into the left ventricle) also improved to a statistically-significant degree with a p-value of 0.04. A p-

value of 0.05 is generally regarded as the threshold for statistical significance (that value implies that there is only a 5% probability that results to which the statistical analysis applies could have arisen by random chance alone).

Other measures of heart pathology improvement exhibiting clinically-meaningful trends if not quite statistically-significant trends. These include impact on the extracellular volume within heart tissue but outside of heart myocytes (p-value was just slightly above the accepted significance threshold of 0.05 at 0.054) & on the intracellular volume with heart myocytes on other heart pathology measures for which p-value was 0.09. Another measure of heart contractility called left ventricular end-diastolic volume (LVEDV; when the left ventricle has not yet pumped out oxygenated blood just received from the left atrium) also exhibited trends to statistical significance without quite getting there, with a p-value of 0.10.

Exhibit 2. Financial Forecast Summary for Cardiol

<i>Year-end December 31</i> <i>(C\$000, exc per share data)</i>	<i>2026E</i>	<i>2027E</i>	<i>2028E</i>	<i>2029E</i>	<i>2030E</i>	<i>2031E</i>	<i>2032E</i>	<i>2033E</i>	<i>2034E</i>	<i>2035E</i>
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)	(\$0.26)	(\$0.23)	(\$0.23)	\$0.07	\$0.43	\$1.17	\$1.93	\$2.29	\$2.72	\$3.15
Fully-taxed EPS (fd)	(\$0.23)	(\$0.20)	(\$0.20)	\$0.06	\$0.38	\$1.03	\$1.69	\$2.02	\$2.39	\$2.77
P/E (basic)	NA	NA	NA	23.8x	4.0x	1.5x	0.9x	0.7x	0.6x	0.5x
EV/EBITDA	NA	NA	NA	9.0x	1.7x	0.6x	0.4x	0.3x	0.3x	0.2x
S/O, basic (M)	94,009	94,009	94,009	94,009	94,009	94,009	94,009	94,009	94,009	94,009
S/O, fd (M)	106,928	106,928	106,928	106,928	106,928	106,928	106,928	106,928	106,928	106,928

Source: Historic data – Cardiol financial filings; Forecasts/Estimates – Leede Financial Inc.

P-value variability is not overly concerning to us - CardiolRx's underlying anti-inflammatory pharmacology was likely impacting all structural heart endpoints with the same mechanism, with all trends favoring CardiolRx if not quite to statistical thresholds in some cases. It does not seem plausible to us at initial data inspection to assume that statistical differences in the various MR-assessed changed in structural heart parameters are relevant mechanistically to CardiolRx's documented impact on inflammatory pathways, including but not limited to the NLRP3 inflammasome pathway for which Cardiol & others provided preclinical evidence either in abstract form or in peer-reviewed manuscripts. As p-values imply, the error bars on CardiolRx's impact on the various measures of heart pathology in comparison to placebo patients were fairly large in most cases (obviously less so for LVM & LAESV, as indicated above) & we would be interested to see in a more granular data analysis if there were any CardiolRx patients who were completely unresponsive to the drug or if most patients did exhibit some responsiveness to CardiolRx, just not on all structural heart measures. Cardiol did not provide any insights on this theme in its recent ARCHER commentary.

We were interested to see in Cardiol's commentary this morning that it made reference to data on left ventricular mass reduction for other cardiovascular-active agents that compare favorably to magnitude of impact just documented for CardiolRx in ARCHER. These include Eli Lilly's (LLY-NY, NR) long-acting GLP-1 analog tirzepatide/Mounjaro for which impact on left ventricular mass was published for the SUMMIT CMR heart failure study in Feb/25 in the *Journal of the American College of Cardiology* & Boehringer Ingelheim's (private) sodium-glucose cotransporter-2 inhibitor drug empagliflozin/Jardiance for which

impact on left ventricular mass was published earlier this quarter in the journal *Biomedicine & Pharmacotherapy*. Cardiol also cited data for Novartis' (NVS-NY, NR) multi-blockbuster valsartan-sacubitril formulation Entresto, for which impact on left ventricle mass has been published in many clinical trials, including but not limited to the REVERSE-LVH trial (in Jul/25 in Nature Communications) & the pivotal PARAGON-HF trial (in Oct/25 in the *Journal of Cardiac Failure*), to name two. In each case, the main focus was on heart failure & not myocarditis, & we would not expect either of these FDA-approved drugs (for which main approved indication is impact on blood glucose modulation) to exhibit any impact on purely inflammatory indications, including myocarditis.

Summary & valuation. We agree with Cardiol & its clinical collaborators that its ARCHER Phase II acute myocarditis data were clinically meaningful, trending positively by some efficacy measures & achieving statistical significance on others. Two structural heart endpoints achieving statistical significance at three-month follow-up in CardiolRx-treated patients as compared to placebo patients, a performance that we consider to be positive on balance for what was still a modestly-sized (by cardiovascular disease clinical trial standards) exploratory Phase II study.

But our viewpoint on Cardiol's ARCHER update is more cautious than enthusiastic, mostly based on signals from the firm & its collaborators that ARCHER data were ironically more positive mechanistically to CardiolRx's prospects in other cardiovascular indications and not directly to acute myocarditis itself. Indeed, the firm provided no details on its path forward in acute myocarditis (timelines to engaging with the US FDA on ARCHER data, expectations on timelines to commencing Phase III acute myocarditis testing, or predictions for Phase III acute myocarditis study design were not provided). Moreover, when asked directly about market size & competitive landscape in acute myocarditis, management's feedback went swiftly to providing those data for recurrent pericarditis & diastolic heart failure, both relevant medical markets in our CRDL model to be sure, but not directly relevant to the acute myocarditis-specific insights that the question addressed. Candidly, we ourselves did not need ARCHER data to give us confidence in CardiolRx/cannabidiol's cardiovascular disease-relevant anti-inflammatory activity - there is far too much mechanistic data in the medical literature, both from Cardiol itself & from independent academic institutions, to give us high confidence in cannabidiol's anti-inflammatory activity, independent of any engagement that this small-molecule has with endocannabinoid receptor pathways with which various cannabinoids (including but not exclusively tetrahydrocannabinol) interact.

Exhibit 3. Valuation Summary for Cardiol

NPV, discount rate		10%	20%	25%	30%	40%	50%
Implied value per share		\$22.22	\$9.99	\$6.87	\$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	\$6.73	\$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}		\$2.92	\$5.95	\$7.46	\$8.97	\$10.49	\$12.00
One-year Cardiol target price (C\$) ¹				\$7.02			

¹ Based on F2031 fd fully-taxed EPS of \$1.03; EBITDA of \$158.0M, discounted at 25%, FD S/O of 106.9M, including Oct/25 equity offering

² Includes pro forma cash \$27.6M (FQ325 cash of \$11.6M, plus US\$11.4M/C\$16.0M gross proceeds from Oct/25 equity offering; no LT debt

Source: Leede Financial Inc.

Revised CardiolRx royalty revenue forecasts now assume that acute myocarditis development timelines will extend beyond those we project for recurrent pericarditis & heart failure. Accordingly, we do believe that ARCHER data are mechanistically validating for CardiolRx's prospects in other inflammation-based cardiovascular diseases (specifically, recurrent pericarditis for which the Phase III MAvERIC trial is actively enrolling riloncept-refractory patients & diastolic heart failure for which IND-enabling studies are ongoing) but Cardiol's implied caution on deploying resources into future acute myocarditis testing gives us corresponding

caution on timelines to funding pivotal Phase III acute myocarditis testing; we are revising our model accordingly. Our model will now assume that Cardiol could conduct pivotal Phase III acute myocarditis testing for CardiolRx during F2027-to-F2029, submitting NDA documentation to the US FDA for the indication in FH230, with CardiolRx FDA approval & US market launch by future partners in FH231 (previously we assumed CardiolRx US launch for acute myocarditis in FH229. Our revised CardiolRx/CRD-38 royalty revenue model is as shown in Exhibit 1.

Financial forecast summary – revising PT to C\$7.00 while preserving Spec Buy rating. In parallel, we are shifting forward the reference year in our EBITDA/fd EPS-based valuation methods to F2031 (was F2030), during which we project EBITDA (as driven by CardiolRx/CRD-38 royalty) of C\$158.0M & fd EPS of C\$1.03/shr, as shown in Exhibits 2 & 3, with our EV calculation incorporating pro forma cash of C\$27.6M (FQ325 cash was C\$11.6M, to which we add net proceeds from the firm's US\$11.0M equity offering consummated after FQ325 concluded) & no LT debt; giving effect to the aforementioned equity offering, we calculate that Cardiol now has fd S/O of 106.9M. Since Cardiol is a Phase III-stage small-molecule drug developer with the MAVERIC/recurrent pericarditis trial already enrolling patients, we believe it is still appropriate for us to use a 25% discount rate in all valuation methods summarized in Exhibit 3, including NPV.

Taking the average of our NPV & discounted EBITDA/fd EPS valuation methods (Exhibit 3), we derive a new one-year PT for CRDL of C\$7.02/shr, which we round to C\$7.00. At current levels our PT corresponds to a one-year return of 443%, a return that may seem aggressive in the wake of yesterday's share price downdraft but still achievable in our view if timelines to MAVERIC data are met later next year & if IND-enabling studies for CRD-38 in diastolic heart failure conclude imminently & if Phase I/II heart failure testing (to which our model ascribes substantial value during F2031-to-F2035 in our NPV valuation) can be well-advanced by end-of-F2026.

We endorse Cardiol's focus on recurrent pericarditis, a market made attractive through riloncept/Arcalyst's commercial success, but acute myocarditis does represent a second indication to which we now ascribe more modest value than originally contemplated. Our valuation aside, we are sympathetic to investor caution on Cardiol's ongoing CardiolRx/CRD-38 R&D activities when legacy programs absorbed a substantial amount of risk capital in prior years including ARCHER, but also the 422-patient Phase II/III COVID-19/cardiovascular adverse event trial (the LANCER trial) that was active in F2021/22 until terminated in late FH222. Data from 90 early enrollees in the trial did not generate a CardiolRx efficacy signal, probably because COVID-19 symptom severity was mitigated by F2022 by availability of anti-viral therapies & vaccine formulations that undoubtedly softened symptom severity from COVID-19 infection, including any cardiovascular-related side effects that may have manifested in naïve patients. And though our model never ascribed material value to Cardiol's commercial cannabidiol/Cortalex sales, Cardiol did feature Cortalex sales as a central operating metric relevant to its investment thesis, at least in its early days as a publicly-traded firm.

Cardiol's clinical collaborators featured myocarditis in their commentary as a side effect from checkpoint inhibition in oncology.

We were interested to hear Cardiol's clinical collaborators speak to the emergence of acute myocarditis as a severe side effect for checkpoint inhibitor therapies used in cancer treatment. The medical literature in fact is well-populated with clinical studies that specifically characterize what is called immune checkpoint-associated myocarditis, recognizing the interrelationship between checkpoint inhibition & myocardium inflammation as a distinct indication. Merck (MRK-NY, NR) in fact identifies in its prescribing information myocarditis as one of the adverse reactions arising from use of its flagship multi-blockbuster anti-PD1 mAb pembrolizumab/Keytruda.

To be fair, myocarditis is one of several adverse reactions identified in Keytruda patients, but nonetheless, myocarditis is one of a few adverse reactions for which Keytruda use should be discontinued if it arises, which speaks to the regard with which myocarditis is held as a monitorable side effect. Prescribing information for Bristol Myers Squibb's (BMY-NY, NR) analogous anti-PD1 mAb nivolumab/Opdivo & Roche's (ROG-SW, NR) anti-PD-L1 mAb atezolizumab/Tecentriq also identify myocarditis as an occasionally observed adverse reaction identified during Phase III testing, though without placing any unique emphasis on myocarditis in comparison to other neurological or cardiovascular events. We believe that the ubiquity with which checkpoint inhibitors are now standard-of-care in many cancer markets could heighten awareness of myocarditis as a niche cardiovascular market for which CardiolRx could be relevant.

A few Phase II/III myocarditis clinical studies are still ongoing, with experimental therapies either based on mitigating inflammation or immune suppression or both. Interestingly, there are a few ongoing Phase II/III acute myocarditis clinical studies independent of ARCHER, with most experimental therapies predictably focused on anti-inflammatory agents targeting the underlying inflammatory pathology of the disease. Relevant active trials are predominantly academic-sponsored studies & usually testing

already-approved anti-inflammatory agents like corticosteroids (methylprednisolone in the 288-patient Phase III MYTHS trial sponsored by Italy-based Niguarda Hospital; six-month cardiovascular event rate data expected by end-of-F2028; also testing methylprednisolone in the 174-patient Phase III MYTHS-MR trial sponsored by Belgium-based Antwerp Hospital; six-month data on improvement in left ventricular ejection volume also expected by end-of-F2028) or the legacy gout drug colchicine (undergoing testing in the 300-patient Phase III ARGO trial sponsored by France-based Assistance Publique, for which six-month cardiovascular composite end-point data are expected by mid-F2028).

Exhibit 4. Comparable Companies For Cardiol

Company	Curr	Sym	Shares out (M)	Share price 1-Dec	Mkt cap (\$M)		Ent val (\$M)		Company description
					(curr)	(C\$)	(curr)	(C\$)	
Cannabinoid drug development peers									
Amarin Corporation PLC	USD	AMRN	415.9	\$15.97	\$6,641	\$9,280	(\$284)	(\$397)	Amarin markets icosapent ethyl capsules Vascepa, aimed at reducing the cardiovascular risk of patients as an add-on therapy with statin
Avicanna Inc	CAD	AVCN	117.8	\$0.24	\$28	\$40	\$41	\$57	Firm announced a partnership with University of Toronto in Jun/20 for the development of a cannabinoid-based treatment for lung inflammation associated with COVID-19.
Applied Therapeutics Inc	USD	APLT	144.3	\$0.26	\$38	\$52	\$38	\$53	Aldose reductase inhibitor AT-001 is targeting diabetic cardiomyopathy with data anticipated from a pivotal Phase III trial by 2022.
Botanix Pharmaceuticals Ltd	AUD	BOT	1,970.7	\$0.12	\$236	\$216	\$586	\$536	BTX-1801, synthetic cannabidiol formulation targeting methicillin-resistant Staphylococcus aureus infection in 60-pt Phase II trial; also BTX 1503 gel, completed Phase II acne trial
Corbus Pharmaceuticals Holdings Inc	USD	CRBP	17.6	\$11.54	\$203	\$185	(\$5)	(\$5)	Corbus' lead asset Lenabasum is an oral synthetic selective cannabinoid receptor type 2 (CB2) agonist, data from a 354-patient Phase III trial for systemic sclerosis failed to show any significant differences on primary and secondary endpoints owing to high placebo response.
Cytokinetics Inc	USD	CYTK	122.3	\$68.13	\$8,330	\$11,639	\$5,142	\$7,184	Lead drug is omecamtiv mecarbil (myotrope; cardiac myosin activation); 8,256-pt Phase III GALACTIC-HF trial (systolic HF) showed benefit on composite CV endpoint compared to placebo (though difference of 37% vs 39.1% was objectively modest), published in <i>NEJM</i> , 2021.
Harmony Biosciences Holdings Inc	USD	HRMY	57.6	\$35.29	\$2,033	\$2,840	\$1,678	\$2,345	Acquired Zynerba in Q423 for US\$60M plus US\$140M in future milestones if achieved; still developing Phase III-stage Zygel, a transdermal cannabinoid formulation for treating Fragile X Syndrome
Mesoblast Ltd	AUD	MSB	1,283.0	\$2.67	\$3,426	\$3,134	\$1,361	\$1,245	Allogeneic mesenchymal stem cell developer; Remestemcel-L for acute graft vs host disease; Revascor (mesenchymal stem cells injected into heart muscle) for chronic heart failure, positive DREAM-HF data in Jan/21
Milestone Pharmaceuticals Inc	USD	MIST	85.2	\$2.69	\$229	\$320	\$110	\$153	Milestone Pharmaceutical's lead is the nasal spray formulation of the calcium channel blocker etripamil for the treatment of patients with PSVT, currently in Phase III testing.
Cardiol Therapeutics Inc	CAD	CRDL	99.5	\$1.29	\$128	\$128	\$101	\$101	CardiolRx/cannabidiol in Phase III recurrent pericarditis MAVERIC trial; data from 109-patient acute myocarditis (ARCHER) trial (Dec/25); IND-enabling testing for injectable CRD-38 in heart failure is ongoing

Source: Company filings, Leede Financial Inc.

Bristol Myers Squibb's T-cell-targeted abatacept/Orencio is not approved for myocarditis but it is undergoing active academic-sponsored Phase II/III testing that could be relevant to myocarditis standard-of-care down the road. One other ongoing Phase III myocarditis trial that caught our eye with regard to myocarditis' relevance in checkpoint inhibition in cancer therapy is the 390-patient ATRIUM trial sponsored by researchers at Massachusetts General Hospital, for which six-month data on myocarditis symptom severity are expected by mid-F2027. The trial is testing the CD80- & CD86-binding fusion protein abatacept, which

by binding to these two T-lymphocyte surface markers impedes T-cell activation, thereby impeding the ability of the patient's immune system to attack heart myocardium. Abatacept is a fusion protein originally developed by Bristol Myers Squibb & branded since 2005 as the rheumatoid arthritis & graft-vs-host-disease (GvHD)-targeted drug Orencio. It is composed of the constant region (Fc) of immunoglobulin IgG1 linked to the extracellular domain of a regulatory T-cell surface protein called cytotoxic T-lymphocyte-associated protein-4 (CTLA-4, which is the target for Bristol Myers Squibb's melanoma-targeted mAb ipilimumab/Yervoy).

Abatacept's prospects for treating checkpoint inhibition-associated myocarditis is already well-characterized in the medical literature, dating back to 2002 before Orencio was yet FDA-approved (a study documenting how blocking signals of T-cell activation could mitigate experimental autoimmune myocarditis was published that year by Japan-based researchers in the *Journal of Molecular & Cellular Cardiology*) & yet Orencio is not yet approved specifically for myocarditis. That trend does appear to be reversing with the aforementioned Phase II/III academic-sponsored studies expected to conclude in a year or two, though interestingly without any overt sponsorship from Bristol Myers Squibb itself.

Independent of the ATRIUM trial, Phase II data from the still-active 21-patient ACHLYS trial could be reported imminently. Study design was published in Feb/25 in the journal *Archives of Cardiovascular Diseases*, showing therein that abatacept is actually part of a combination therapy that includes the Janus kinase inhibitor drug ruxolitinib (Incyte's [INCY-Q, NR] Jakafi) & corticosteroids, with primary endpoints focused on three-month impact on various markers of systemic immune activation. But we do not see any corporate-sponsored clinical studies testing other immunologically active agents in acute myocarditis, not even by rilonacept/Arcalyst developer Kiniksa (KNSA-Q, NR) that is the market leader in recurrent pericarditis, the indication for which Cardiol is advancing its own CardiolRx-directed Phase III program & for which acute myocarditis is pathologically distinct but still mechanistically similar as suggested by Cardiol's own ARCHER data. In fact, Kiniksa is not funding any Phase II-to-IV rilonacept clinical studies at all, with only one rilonacept clinical study ongoing & not with any overt participation from Kiniksa itself (the US-based Mayo Clinic is funding a 60-patient Phase II rilonacept trial in cardiac sarcoidosis).

Disclosures none

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