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CRDL-TSX, CRDL-NASDAQ

Rating:	Speculative Buy
Target:	$11.00
Price:	$1.85
Return:	495%
Valuation:	NPV, 20x EPS, 12.5x EV/EBITDA (F2030 estimates, 25% disc)

Market Data

Basic Shares O/S (M)	82.6
FD Shares O/S (M)	89.8
Market capitalization ($M)	152.8
Enterprise Value ($M)	129.5
Pro forma cash ($M, Inc Oct/24 offer)	23.3
LT debt ($M, most rec Q)	0.0
52 Week Range	$1.09-$3.57
Avg. Weekly Volume (000)	437,654
Fiscal Year End	31-Dec

Key Milestones (Calendar Year)

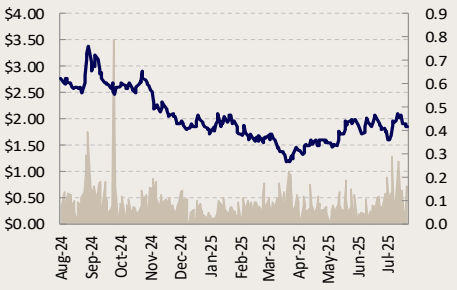
CardiolRx, PhII pericarditis data (pilot-MAvERIC), Jun/24	Q224
CardiolRx, commence Phase II/III pericarditis trial (MAvERIC), Apr/25	Q125
CardiolRx, PhII myocarditis data (ARCHER), Aug/25	Q325
CRD-38, IND filing for heart failure with preserved eject fract (HFpEF)	H225

Financial Metrics

In C$000	2028E	2029E	2030E
Rev, acute myocarditis	$0	$33,174	$83,432
Rev, recur pericarditis	$0	$32,597	$81,981
Rev, HFpEF	$0	$0	$0
Total Revenue ($000)	$0	$65,770	$165,413
EBITDA ($000)	($20,618)	$42,659	$139,269
Adj net inc ($000)	($21,721)	$29,089	$96,717
EPS (basic)	($0.26)	$0.35	$1.17
EPS (FD)	($0.24)	$0.32	$1.08

Company Description

Cardiol Therapeutics is an ON-based cardiovascular disease drug developer, focused on developing ultrapure cannabidiol formulation CardiolRx in inflammatory heart diseases, specifically recurrent pericarditis, acute myocarditis, & diastolic heart failure (HFpEF).



Source: Refinitiv, Leede Financial

ARCHER Data. Clear Evidence Of CardiolRx's Anti-Inflammatory Activity In Acute Myocarditis Justifies Further Clinical Testing In Our View – Spec Buy

ON-based small-molecule cardiovascular disease drug developer Cardiol Therapeutics reported headline Phase II data for its 109-patient acute myocarditis study (the ARCHER trial) testing the firm's orally-active ultra-pure synthetic cannabidiol formulation CardiolRx for the indication. Patient enrollment for the twelve-week trial concluded back in late FQ324 & so we were anticipating final data analysis sometime during FQ225, a timeline that slipped only marginally into FQ325.

ARCHER data deemed favorable by Cardiol & its collaborators on at least one primary endpoint, but abundant biomarker & cardiac function data are still pending. Cardiol's ARCHER update was heavy on description and light on actual data, and to be candid, we suspect that capital market response to the ARCHER data is that it is largely devoid of ARCHER data, an observation made even more stark by the fact that the primary endpoints were based on three-month follow-up analysis of a study that completed enrollment back in late Sept/24 as indicated above. The trial has two primary endpoints, one of which was essentially met though not quite to a statistically significant degree (cardiac MR-assessed change in extracellular volume) & another that was not met (global longitudinal strain, also assessed by cardiac MR) but which had no chance of being met based on patient enrollment characteristics, as we will describe.

Capital markets invariably exhibit limited tolerance for missing a statistical significance threshold & that appears to be impacting CRDL share value today, notwithstanding commentary from collaborating cardiologists. So on the press-released ARCHER update itself, Cardiol indicated that CardiolRx-treated patients exhibited measurable improvement on extracellular volume on cardiac MR images after three months of CardiolRx in comparison to placebo patients, with a p-value that was close to achieving statistical significance (p-value was 0.054, close to 0.05 & still reflecting to us that CardiolRx exhibited clear efficacy trends).

We assume that the variable being measured is the mean (or median) magnitude of MR-confirmed extracellular volume reduction in CardiolRx vs placebo patients & not the absolute number of patients who were categorized as responders by experiencing a magnitude of extracellular volume reduction below a specified threshold. Indeed, our review of ARCHER trial design that was published last year by Cardiol & its clinical collaborators in *ESC Heart Failure* indicates to us that the former interpretation is the most reasonable characterization of Cardiol's extracellular volume analysis.

As an aside, today's share price performance is in a way unsurprising when just considering the slight (and we emphasize slight) miss on achieving statistical significance on extracellular volume reduction (a measure of reduced myocardium inflammation/fibrosis). We have rarely if ever seen capital markets express tolerance for missing statistical significance even when considering compounding factors like the magnitude of the miss (extremely small in ARCHER) or trial size (109 patients in ARCHER is not trivial, but it is not powered to a level that would be necessary for a pivotal Phase III registration study either) or target indication (acute myocarditis, for which assessing efficacy involves interpretation of radiographic images, not hard

endpoints as in oncology [survival] or infectious disease [microbial load is either reduced or it is not]) or nature of standard-of-care (there is really no approved pharmacopeia for myocarditis other than off-label use of glucocorticoids or anti-hypertensive agents).

Exhibit 1. CardiolRx (In Acute Myocarditis & Recurrent Pericarditis) & CRD-38 (Diastolic Heart Failure, 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%*	*10.0%*	*25.0%*	*30.0%*	*40.0%*	*50.0%*	*55.0%*	*60.0%*
Gross revenue, CardiolRx (US$000)	$0	$0	$0	$113,415	$285,238	$344,340	$461,874	$580,807	$642,721	$705,357
Gross revenue, CardiolRx (C$000)	$0	$0	$0	$147,439	$370,810	$447,641	$600,436	$755,049	$835,537	$916,964
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	$110,579	$278,107	$335,731	$450,327	$566,287	$626,653	$687,723
Royalty rate on net sales (%)	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
CardiolRx (Myocarditis), royalty rev (C$000)	**$0**	**$0**	**$0**	**$33,174**	**$83,432**	**$100,719**	**$135,098**	**$169,886**	**$187,996**	**$206,317**
Recurrent Pericarditis, US										
Current Population, United States	342,130,165	344,182,946	346,248,043	348,325,532	350,415,485	352,517,978	354,633,086	356,760,884	358,901,449	361,054,858
Annual incidence, acute pericarditis	94,770	95,339	95,911	96,486	97,065	97,647	98,233	98,823	99,416	100,012
Proportion, recurrent pericarditis	31,274	31,462	31,651	31,840	32,031	32,224	32,417	32,612	32,807	33,004
Proportion, second-third-fourth recurrence	10,946	11,012	11,078	11,144	11,211	11,278	11,346	11,414	11,483	11,551
Price per treated patient (US$)	$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**	**$126,705**
Diastolic Heart Failure, US										
Current Population, United States	342,130,165	344,182,946	346,248,043	348,325,532	350,415,485	352,517,978	354,633,086	356,760,884	358,901,449	361,054,858
Heart failure prevalence, all subcategores	6,737,538	6,777,963	6,818,631	6,859,543	6,900,700	6,942,104	6,983,757	7,025,660	7,067,814	7,110,220
Prevalence, diastolic heart failure (HFpEF)	3,368,769	3,388,982	3,409,316	3,429,772	3,450,350	3,471,052	3,491,879	3,512,830	3,533,907	3,555,110
Annual incidence, diastolic heart failure (HFpEF)	285,050	286,760	288,481	290,211	291,953	293,704	295,467	297,239	299,023	300,817
Price per annual course of therapy (US$)	$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**	**$65,770**	**$165,413**	**$250,888**	**$337,676**	**$403,762**	**$445,141**	**$487,002**

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

CardiolRx does not impact a separate measure of cardiac function, global longitudinal strain, but this measure of left ventricle pathology was normal at enrollment & thus was minimally relevant to CardiolRx's impact on disease. As also described in the 2024 *ESC Heart Failure* paper, another measure of myocardial function that was assessed in ARCHER was so-called global longitudinal strain (GLS), which like extracellular volume is also assessed through interpretation of cardiac MR images and which did not show any efficacy trends in CardiolRx-treated patients at three-month follow-up. As the name implies, GLS is a measure of how well the heart's left ventricle is contracting along its vertical axis, from the mitral valve through which the left ventricle receives oxygenated blood down to its apex at the bottom, and as stated above, this too is assessed through cardiac MR image analysis. The extent to which the left ventricle lengthens & shortens during a contraction cycle is quantified through image

analysis to determine efficiency of left ventricle function. GLS is commonly measured in cardiovascular studies, including but not limited to myocarditis studies & is frequently quantified in Phase II/III studies where cardiac toxicity of other agents (for example, anti-cancer agents) is being assessed as a side effect.

Exhibit 2. Financial Forecast Summary for Cardiol

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	$33,174	$83,432	$100,719	$135,098	$169,886	$187,996	$206,317
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**	**$65,770**	**$165,413**	**$250,888**	**$337,676**	**$403,762**	**$445,141**	**$487,002**
Revenue growth (%)	*NA*	*NA*	*NA*	*NA*	*252%*	*152%*	*135%*	*120%*	*110%*	*109%*
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	$17,864	$20,767	$22,254	$22,927	$22,323	$22,919	$23,531
Other expenses	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
EBITDA	**($23,541)**	**($20,765)**	**($20,618)**	**$42,659**	**$139,269**	**$223,125**	**$309,107**	**$375,658**	**$416,299**	**$457,403**
EBITDA growth (%)	(5%)	(12%)	(1%)	(307%)	226%	60%	39%	22%	11%	10%
EBITDA margin (%)	*NA*	*NA*	*NA*	*65%*	*84%*	*89%*	*92%*	*93%*	*94%*	*94%*
Non-operating expenses	$719	$719	$719	$719	$719	$719	$719	$719	$719	$719
EBIT	**($24,260)**	**($21,484)**	**($21,337)**	**$41,940**	**$138,550**	**$222,406**	**$308,388**	**$374,939**	**$415,580**	**$456,684**
Other non-oper expenses	$384	$384	$384	$384	$384	$384	$384	$384	$384	$384
EBT	**($24,643)**	**($21,867)**	**($21,721)**	**$41,556**	**$138,167**	**$222,022**	**$308,004**	**$374,555**	**$415,196**	**$456,300**
Tax expense	$0	$0	$0	$12,467	$41,450	$66,607	$92,401	$112,366	$124,559	$136,890
Net income, fully-taxed	($24,643)	($21,867)	($21,721)	$29,089	$96,717	$155,416	$215,603	$262,188	$290,637	$319,410
Fully-taxed EPS (basic)	($0.30)	($0.26)	($0.26)	$0.35	$1.17	$1.88	$2.61	$3.17	$3.52	$3.87
Fully-taxed EPS (fd)	**($0.27)**	**($0.24)**	**($0.24)**	**$0.32**	**$1.08**	**$1.73**	**$2.40**	**$2.92**	**$3.24**	**$3.56**
P/E (basic)	*NA*	*NA*	*NA*	*5.7x*	*1.7x*	*1.1x*	*0.8x*	*0.6x*	*0.6x*	*0.5x*
EV/EBITDA	*NA*	*NA*	*NA*	*3.0x*	*0.9x*	*0.6x*	*0.4x*	*0.3x*	*0.3x*	*0.3x*
S/O, basic (M)	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*	*82,609*
S/O, fd (M)	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*	*89,828*

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

ARCHER notwithstanding, we would like to see how well CardiolRx impacts GLS in a myocarditis patient population that actually exhibited left ventricular dysfunction at enrollment, just to more fully explore CardiolRx's mode of action. Though it is common to analyse GLS in a cardiovascular function study like ARCHER, it seems to have been an irrelevant parameter to quantify in this study if only because all of the enrolled subjects exhibited preserved left ventricular ejection fraction at enrollment & so exhibited normal physiology on this metric even before CardiolRx (or placebo) administration.

There was no indication in the 2024 *ESC Heart Failure* review of ARCHER design nor in the US NIH clinical database summary of ARCHER that acute myocarditis patients would necessarily have preserved left ventricle function at enrollment, so in a way, it would have been evidence of CardiolRx's ineffectiveness on mitigating myocarditis symptoms if it impacted GLS in patients with otherwise normal left ventricle ejection fraction.

ARCHER has no less than seventeen other secondary endpoints related to quantifying cardiac biomarkers or other measures of heart physiology for which tangible data are not yet in the public domain & we look forward to more quantitative analysis of these secondary endpoints when Cardiol presents ARCHER data in a formal scientific venue. In the interim, we are encouraged by Cardiol's qualitative statement that MR-confirmed reduction in extracellular volume was also associated with improvements in other MR-confirmed endpoints, including but not limited reduction in left ventricle mass (higher mass is associated with lower ejection fraction).

Our analysis of ARCHER will remain incomplete until we have tangible cardiopathology data to review, perhaps as early as at the ESC Congress 2025 meeting later this quarter (so we assume). Cardiol did not indicated where/when it expects to share tangible ARCHER data but we assume based on imminence alone that the occasion will be the ESC Congress 2025 meeting in Spain at the end-of-Aug/25. The alternative conference would be the annual American Heart Association meeting in Nov/25 (where Cardiol presented data from its 27-patient Phase II recurrent pericarditis [pilot-MAvERIC] trial last year) but we believe that Cardiol understands the need to disclose tangible ARCHER data much earlier than in mid-FQ425. If our assumption is

correct, we expect to have ARCHER data available to us for more rigorous review later this quarter. It is clear though from commentary in the ARCHER press release today that Cardiol's clinical collaborators believe that CardiolRx performed to expectations in ARCHER and that data available to them is sufficiently positive in their view to justify advancing into more substantial Phase II/III acute myocarditis CardiolRx testing. We are not yet able to independently reach that conclusion, but clinical collaborators have and in so doing remain positive about CardiolRx's prospects in this indication.

Exhibit 3. Valuation Summary for Cardiol

NPV, discount rate		10%	20%	25%	30%	40%	50%
Implied value per share		$29.36	$14.92	**$9.81**	$7.72	$3.89	$1.74
Price/earnings multiple, 2030E		**10%**	**20%**	**25%**	**30%**	**40%**	**50%**
Implied share price[1]	10	$8.67	$6.68	$5.91	$5.25	$4.21	$3.42
	20	$17.34	$13.36	**$11.03**	$10.50	$8.42	$6.84
	30	$26.01	$20.04	$17.73	$15.75	$12.63	$10.26
EV/EBITDA multiple, 2030E		**5x**	**10x**	**12.5x**	**15x**	**17.5x**	**20x**
Implied share price[1,2]		$5.99	$12.20	**$12.82**	$18.40	$21.50	$24.60
One-year Cardiol target price (C$) [1]				**$11.22**			

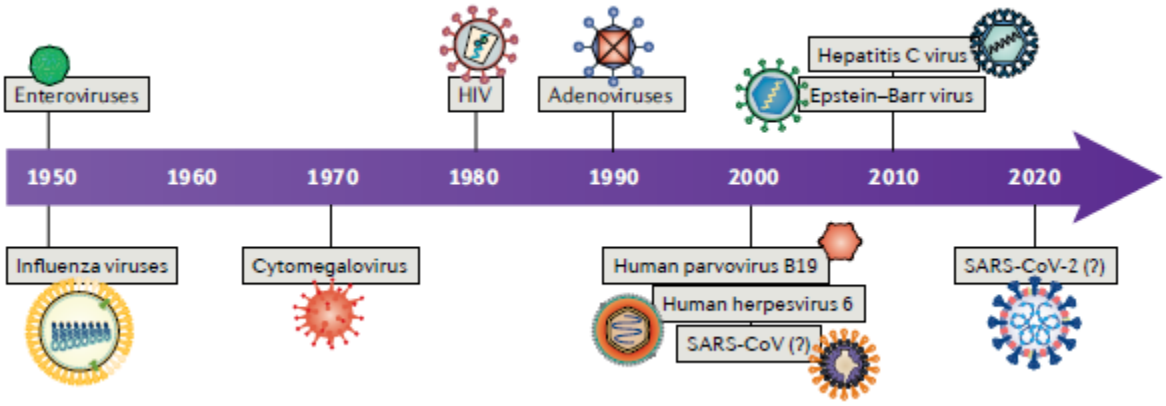
[1] *Based on F2030 fd fully-taxed EPS of $1.08; EBITDA of $139.3M, discounted at 25%, FD S/O of 89.8M, including Oct/24 equity offering*

[2] *Includes FQ125 cash of $23.3M and no LT debt*

Source: Leede Financial Inc.

Summary & valuation. We are disinclined to materially revise our CRDL investment thesis in the wake of Cardiol's ARCHER update based on the fact that: (1) we believe that a trial that only misses statistical significance in the third decimal place has performed to a sufficiently high clinical standard to justify further testing, as already predicted in our model & (2) we have abundantly positive commentary on ARCHER performance from enrolling physicians, but (3) we are still awaiting dissemination of tangible secondary endpoint data for us to independently review; accordingly, our ability to derive our own interpretation of ARCHER data is still pending.

Exhibit 4. Prominent Viruses Associated With Inflammatory Cardiomyopathies, Including Myocarditis, Over Time



Source: *Nature Reviews Cardiology (2021). Vol. 18, pp. 169-193*

We certainly could revise our valuation by upwardly revising the discount rate that we incorporate into our NPV & discounted earnings valuation methods, but we believe that 25% is reasonable for what is already a Phase III-stage cardiovascular drug developer (the 110-patient Phase III recurrent pericarditis trial [the MAvERIC trial] testing CardiolRx in patients who discontinued therapy with interleukin-1-blocking therapies like rilonacept/Arcalyst enrolled its first patients in April/25). Upon revisiting our

projected timelines for CardiolRx to complete Phase III testing in the three indications to which we ascribe value (acute myocarditis, recurrent pericarditis & diastolic heart failure [HFpEF]), our royalty revenue forecasts for orally-administered CardiolRx & for subcutaneously-injected CRD-38 (both cannabidiol-based) are as revised & summarized in Exhibits 1 & 2.

We are maintaining our Speculative Buy rating & one-year PT for CRDL of C$11.00, based on NPV determination (25% discount rate as indicated above) and multiples of our F2030 EBITDA/fd EPS forecasts of C$139.3M & C$1.08/shr, respectively. Previously we based our CRDL valuation in part on our F2028 EBITDA/fd EPS forecasts that we have independently revised based on our current projections for timelines to CardiolRx/CRD-38 FDA approval/launch in their respective US cardiovascular disease markets. Our EV calculation incorporates Cardiol's FQ125 balance sheet data (cash of $23.3M, no LT debt) & fd S/O of 89.8M. Our royalty rate & pricing assumptions for CardiolRx & CRD-38 and our foundational epidemiological assumptions for Cardiol's target markets are all unchanged, as shown in Exhibit 1.

Exhibit 5. Comparable Companies For Cardiol

Company	Curr	Sym	Shares out (M)	Share price 6-Aug	Mkt cap ($M) (curr)	Mkt cap ($M) (C$)	Ent val ($M) (curr)	Ent val ($M) (C$)	Company description
Cannabinoid drug development peers									
Amarin Corporation PLC	USD	AMRN	20.7	$15.13	$313	$431	($284)	($391.5)	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	114.2	$0.28	$32	$44.0	$41	$56.1	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	141.6	$0.48	$67	$92.7	$38	$52.5	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	1,961.1	$0.15	$294	$262	$545	$485.7	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	12.2	$8.90	$109	$97	($5)	($4.8)	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 signifncant differences on primary and secondary endpoints owing to high placebo response.
Cytokinetics Inc	USD	CYTK	119.4	$36.16	$4,318	$5,947.4	$5,142	$7,081.1	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 *NEJM, 2021.*
Harmony Biosciences Holdings Inc	USD	HRMY	57.4	$34.94	$2,006	$2,763.2	$1,678	$2,311.5	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	1,280.0	$2.43	$3,110	$2,771.3	$810	$721.4	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	85.0	$1.54	$131	$180.2	$110	$150.9	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**	**82.7**	**$1.85**	**$153**	**$153**	**$130**	**$129.7**	**(CardiolRx/cannabidiol performs well in 25-patient recurrent pericarditic trial (Pilot-MAvERIC; Jun/24); solid data in100-patient acute myocarditis (ARCHER) trial (Aug/25); preclinical heart failure (HFpEF) data for injectible CRD-38 (*JACC* Feb/25)**

Source: Company filings, Leede Financial Inc.

Cardiol now has three distinct cardiovascular indications for which its high-purity cannabidiol formulations exhibited anti-inflammatory activity that translated into physiological benefit. Recall that Cardiol provided two separate updates on CardiolRx/CRD-38 in recent months, including its update on CardiolRx performance in pilot-MAvERIC/recurrent pericarditis, showing in that 27-patient open-label trial that CardiolRx-treated patients exhibited sustained pain relief (as quantified by the eleven-point numerical rating scale [NRS]) for at least six-months, with an average pain score at enrollment of 5.8 for all 27 patients declining to 1.5 at six-month follow-up. We considered these data then as we do now as encouraging not just in absolute magnitude of chest pain relief but also when compared to interim data reported at two-month follow-up at the end-of-FQ224 that showed a reduction in NRS score down from the same baseline to 2.1, showing that CardiolRx symptomatic relief in pericarditis patients was sustained after CardiolRx administration was discontinued & that measurable improvement in pain scores transpired thereafter. Though CardiolRx was not directly compared to Kiniksa's (KNSA-Q, NR) FDA-approved anti-interleukin-1-blocking biologic rilonacept/Arcalyst in a distinct randomized study arm but pilot-MAvERIC data did compare favorably to data at equivalent time points as published in the *New England Journal of Medicine* by Kiniksa for the twelve-week 86-patient RHAPSODY trial.

And as we described back in Feb/25 in our Healthcare Weekly, Cardiol now has substantial preclinical data establishing the medical prospects for its elastin polypeptide-formulated injectible cannabidiol formulation CRD-38, nicely showing in an animal model of diastolic heart failure (mice that were injected with the nitric oxide synthase inhibitor N-nitro-L-arginine methyl ester [L-NAME]) systemically injected CRD-38 improved multiple heart failure symptoms, including ejection fraction, myocyte area, reduction in heart muscle fibrosis & improved stroke volume & ejection fraction. Interestingly, Cardiol separately showed that the nuclear receptor protein peroxisomal proliferator-activated receptor gamma (PPAR-ɣ) could be relevant to CRD-38's mode of action in heart failure & to a degree that is more relevant than the CF1/CB2 cannabinoid receptor pathways with which the drug separately interacts. Preclinical data published on a distinct animal model for recurrent pericarditis nicely showed that cannabidiol's mode of action in this indication could be through the NLRP3 inflammasome pathway, thus featuring the pharmacologic diversity that this cannabinoid exhibits and in ways that are independent of other cannabinoids for which CNS activity is more prevalent. These data were published that month in the *Journal of the American College of Cardiology*.

As one last observation, we were interested to see that ARCHER collaborator & Mayo Clinic-based cardiologist LT Cooper noted in his press release commentary that myocarditis is an increasingly diagnosed consequence of anti-cancer therapies that include anti-PD1 or anti-PD-L1 checkpoint inhibitor mAbs like Merck's (MRK-NY, NR) pembrolizumab/Keytruda or Roche's (ROG-SW, NR) atezolizumab/Tecentriq or anti-CTLA-4 mAbs like Bristol Myers Squibb's ipilimumab/Yervoy, for which myocarditis is frequently encountered. The myocarditis-checkpoint inhibition connection is well-characterized in the medical literature in fact, nicely summarized for example in a *Frontiers in Immunology* review published in Apr/25 by Sichuan University researchers & indeed, myocarditis that is tightly associated with checkpoint inhibition is frequently designated in the medical literature as immunotherapy myocarditis. Since use of immunologically-active checkpoint inhibitors is certainly growing (Keytruda is easily the most highly-prescribed injectible therapy in global oncology markets at present; FQ225 sales were US$8.0B) and not shrinking, it seems plausible to assume that myocarditis incidence could grow in lockstep beyond cardiovascular medical markets and into oncology markets as well.

Disclosures none

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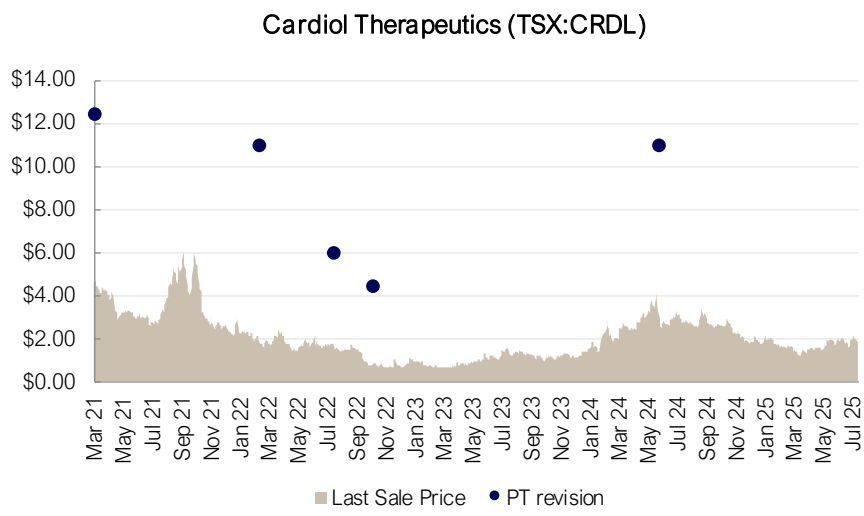
Buy	7	41%
Speculative Buy	8	47%
Hold	1	6%
Sell	-	-
Tender	1	6%
Under Review	-	-

Historical Target Price



Date	Target ($)	Rating
25 Mar 2021	C$12.50	Spec Buy
1 Mar 2022	C$11.00	Spec Buy
3 Aug 2022	C$6.00	Spec Buy
26 Oct 2022	C$4.50	Spec Buy
13 Jun 2024	C$11.00	Spec Buy

Coverage Initiated: Mar 25, 2021

Data sourced from: Refinitiv