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## Hillstream BioPharma (HILS) – Initiating with a Buy rating and \$4.0 Price Target

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**Jason H. Kolbert**  
Managing Director & Senior Analyst  
jkolbert@dawsonjames.com

### Early but Promising Oncology Platform - Ferroptosis

*Hillstream bio is an early-stage biotech company about to enter the clinic this year. The company is investigating ferroptosis, an emerging anti-cancer mechanism that produces iron-mediated cell death – IMCD. The company’s most advanced product candidate is HSB-1216, an IMCD inducer targeting various solid tumors. Hillstream’s goal is to submit an investigational new drug application to the FDA in 2023 in advance of a clinical study set to follow. While this company is “early,” we find the technology promising and the valuation low.*

### Investment Thesis

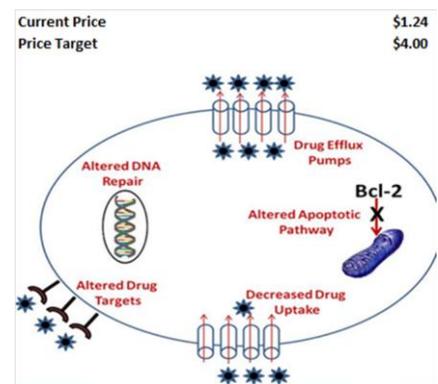
**Early but Promising:** Ferroptosis, or iron-mediated cell death - IMCD, is an emerging regulated cell death process that decreases intracellular iron or the Labile Iron Pool LIP. Cancer cells increase the LIP leading to unregulated cell growth and metabolism. Decreasing the LIP induces iron-led ROS production and lipid peroxidation, two key hallmarks of ferroptosis/IMCD. HSB-1216 binds to iron in the cytoplasm of cancer cells and decreases the LIP, thereby inducing ferroptosis/IMCD, leading to regulated cell death. Areas of interest for the development of HSB-1216 are as a treatment of solid tumors, including TNBC, uveal melanoma, glioblastoma multiforme, head and neck squamous cell carcinoma, and other treatment-resistant cancers with high unmet needs.

**Reaching the Tumor Microenvironment TME: Quatramer represents the company’s delivery to reach the TME while sparing healthy tissue.** This is accomplished by efficiently extending the circulation half-life, combined with targeted delivery to the tumor site; Quatramer traps drugs into the TME. This emerging orthogonal anti-cancer approach utilizes a fundamental recognized mechanism of iron-mediated tumor growth and metabolism.

**TridentAI: Artificial Intelligence Precision Medicine Platform:** TridentAI integrates diverse public datasets such as the Cancer Genome Atlas to identify novel gene signatures to stratify patients prospectively in clinical trials. Quatramer tumor targeting also allows patients to be segmented by using the data to (i) synthetic lethal sensitivities with novel combinations, (ii) pursue undruggable targets such as c-myc, and (iii) target tumors with a high degree of cell plasticity indicative of recurrent/drug-resistant phenotype.

**Valuation:** We project our model out to 2033. We apply a 30% risk cut to our projected revenues in our product model in addition to our 30% risk rate applied in our Free Cash Flow to the Firm (FCFF), discounted EPS (dEPS), and Sum-of-the-Parts (SOP) models. We use a fully diluted out-year share count, assuming multiple raises. The result is equal-weighted, averaged, and rounded to the nearest whole number to derive our 12-month projected price target of \$4.0.

**Risks to our thesis include:** 1. Regulatory Approvals; 2. Clinical Science 3. Adoption Rates 4. The competitive landscape. 5. Intellectual Capital 6. Dilution.



Current Price	\$1.24
Price Target	\$4.00
Source: Hillstream	
Stock Data	
52-Week Range	\$0.30 - \$2.78
Shares Outstanding (mil.)	11.5
Market Capitalization (mil.)	\$14
Enterprise Value (mil.)	\$7
Debt to Capital	0%
Book Value/Share	-
Price/Book	#N/A
Average Three Months Trading Volume (K)	14
Insider Ownership	65.7%
Institutional Ownership	0.7%
Short interest (mil.)	0.1%
Dividend / Yield	\$0.00/0.0%



**Company Description:** (adapted from the company's filings): Hillstream BioPharma is a pre-clinical biotechnology company developing novel therapeutic candidates targeting ferroptosis, an emerging new anti-cancer mechanism resulting in iron-mediated cell death ("IMCD") for treatment-resistant cancers. The most advanced product candidate that Hillstream owns is HSB-1216, an IMCD inducer targeting a variety of solid tumors. Hillstream's goal is to submit an investigational new drug application to the FDA in 2023 and start a clinical study with HSB-1216 in 2023. The HSB-1216 clinical study plans to focus on expanding upon an earlier clinical pilot study conducted in Germany. If Hillstream can start its clinical study with HSB-1216 in 2023, they anticipate that initial clinical data from this trial will be released at either the end of 2023 or early 2024. The company plans to use its Quatramer proprietary tumor targeting platform to enhance the uptake of HSB-1216 in the tumor microenvironment with an extended duration of action and minimal off-target toxicity. The company plans to leverage its TridentAI, - an artificial intelligence precision medicine platform, to identify biomarkers in its clinical programs to better target specific patient segments likely to respond to therapy.

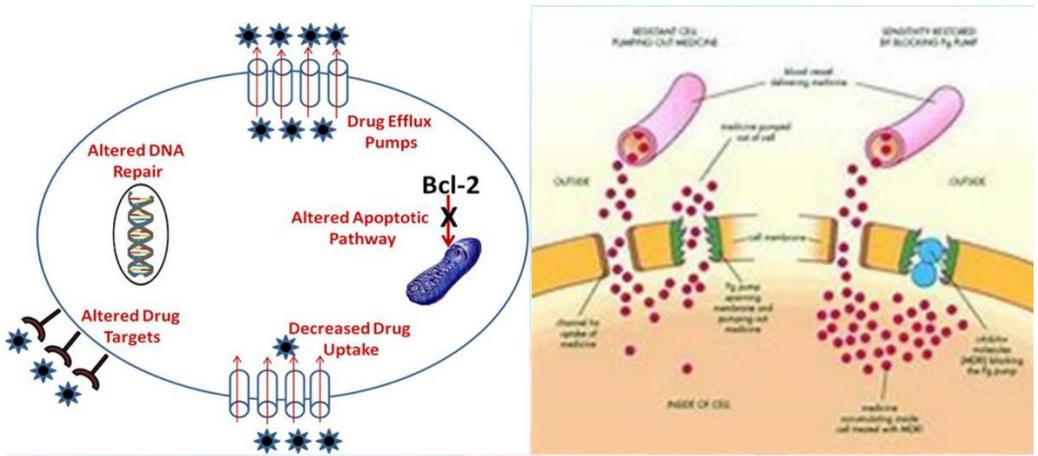
**Exhibit 1. Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020.**

<p><i>The most common in 2020 (in terms of new cases of cancer) were:</i></p> <ul style="list-style-type: none"> <li>• <b>breast</b> (2.26 million cases)</li> <li>• <b>lung</b> (2.21 million cases)</li> <li>• <b>colon and rectum</b> (1.93 million cases)</li> <li>• <b>prostate</b> (1.41 million cases)</li> <li>• <b>skin</b> (non-melanoma) (1.20 million cases)</li> <li>• <b>stomach</b> (1.09 million cases)</li> </ul>	<p><i>The most common causes of cancer death in 2020 were:</i></p> <ul style="list-style-type: none"> <li>• <b>lung</b> (1.80 million deaths)</li> <li>• <b>colon and rectum</b> (916,000 deaths)</li> <li>• <b>liver</b> (830,000 deaths);</li> <li>• <b>stomach</b> (769,000 deaths)</li> <li>• <b>breast</b> (685,000 deaths)</li> </ul>
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**93% of failures in chemotherapy are during the invasion and metastasis of cancer related to drug resistance.**

Source: Hillstream BioPharma.

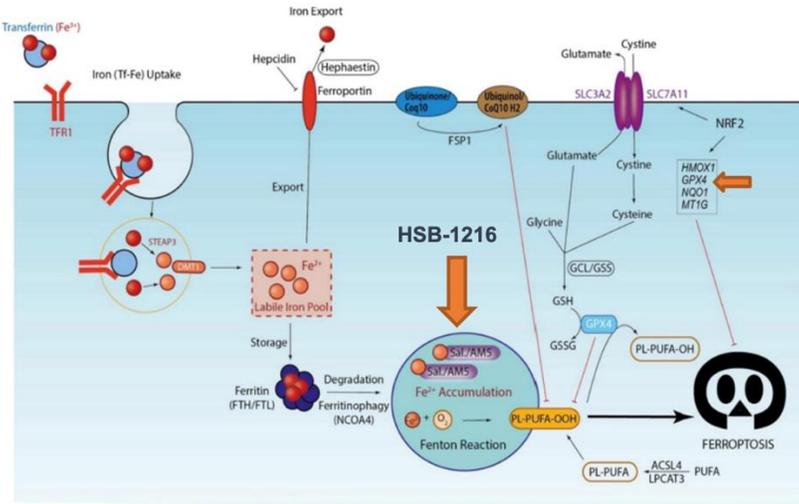
**Exhibit 2. Drug-Resistant Cancers are Rising too.**



Cancer cells resist treatment by expelling cancer treatment drugs (drug efflux pumps). Molecular alterations that contribute to intrinsic or acquired treatment resistance include mutation of the drug's molecular target, changes in the way the drug interacts with the tumor, broad cellular changes, and changes in the tumor microenvironment. Cancer cells may adapt to the drugs while it is being administered, acquiring molecular changes that allow them to escape the effects and acquire resistance. Molecular changes that make cancer insensitive to a particular drug before treatment even begins; it is possible within the same tumor often have a variety of molecular changes called intrinsic resistance.

Source: Hillstream BioPharma

**Exhibit 3. Ferroptosis: An iron-mediated cell death:** Ferroptosis is an emerging anti-cancer mechanism that involves a programmed cell death that is dependent on iron and characterized by the accumulation of lipid peroxides. Ferroptosis is genetically and biochemically distinct from other forms of regulated cell death, such as apoptosis.



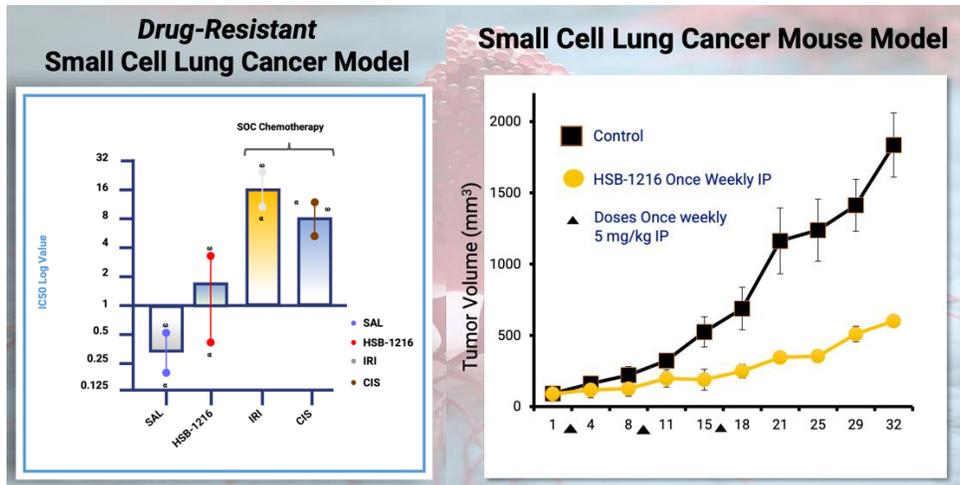
Source: Hillstream BioPharma

**Exhibit 4. HSB-1216, and IMCG modulator, uses Ferroptosis to target drug-resistant cancer cells**



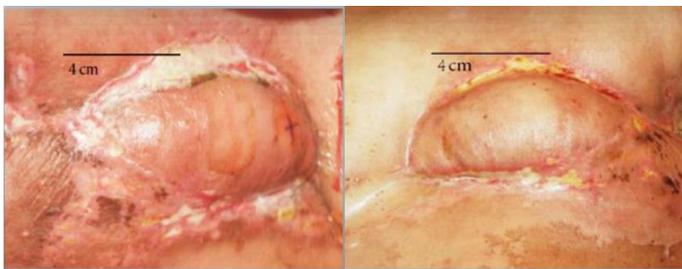
Source: Hillstream BioPharma

Exhibit 5. HSB-1216 Chemo-Resistant Tumors in pre-clinical models



Source: Hillstream BioPharma

**Exhibit 6. HSB-1216 Shows Promise. HSB-1216 had a 71% Response rate during the first-in-man clinical study.** Five of seven solid tumors patients with metastatic breast, ovarian, head, and neck cancers, of which were heavily pre-treated and therapy-resistant tumor types, showed regression in the tumor mass with HSB-1216



Source: Hillstream BioPharma

Exhibit 7. The Pipeline

	Candidate	Mechanism	Indication	Pre-clinical	IND Enabling	Phase 1	Phase 2	Phase 3
	<b>HSB-1216</b>	Ferroptosis / Iron Mediated Cell Death (IMCD)	Solid tumors		Clinical Pilot Study (Germany)			
	<b>HSB-888</b>	Synthetic Lethality HSB-1216 & novel anthracycline	Sarcomas					
	<b>HSB-510</b> (NCATS-NIH CRADA)	Targets PI3K-delta & HDAC6 (inhibits c-myc)	Solid tumors & Lymphomas					
	<b>HSB-114</b>	TNF-alpha DNA	Metastatic Soft Tissue Sarcoma					

Source: Hillstream BioPharma

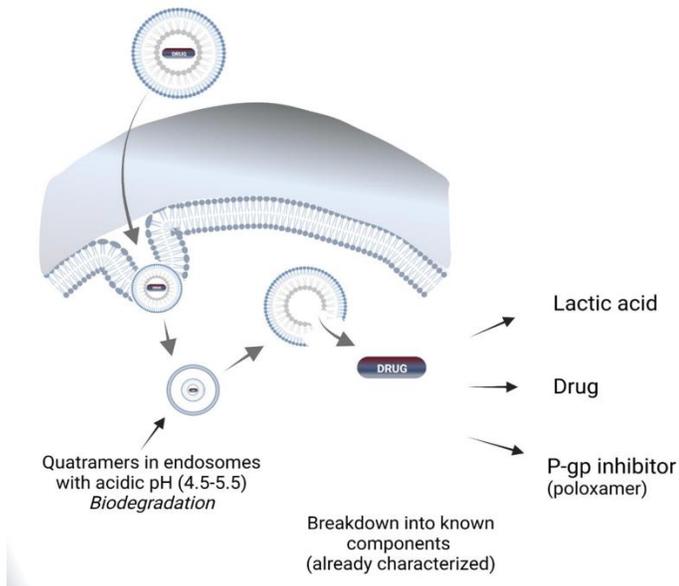
Exhibit 8. The Pipeline (continued)

### Pipeline Drugs with Novel MoA & Focused on Unmet Medical Needs

	Candidate	Mechanism	Indication	Pre-clinical	IND Enabling	Phase 1	Phase 2
	<b>HSB-1216<sup>1</sup></b>	Ferroptosis / Iron Mediated Cell Death (IMCD) <i>Orphan Drug Designation (ODD)</i>	Solid tumors	Clinical Pilot Study	2H 2022: Start POC Trial First Patient In	1H 2023: Initial data POC and submit IND	2023: Start Phase 1
	<b>HSB-888<sup>2</sup></b>	Synthetic Lethality HSB-1216 & novel anthracycline <i>Orphan Drug Designation (ODD)</i>	Sarcomas				
	<b>HSB-510<sup>3</sup></b> (NCATS-NIH CRADA)	Targets PI3K-delta & HDAC6 (inhibits <i>c-myc</i> )	Solid tumors & Lymphomas				
	<b>HSB-114<sup>4</sup></b>	TNF-alpha DNA	Metastatic Soft Tissue Sarcoma				

Source: Hillstream BioPharma

### Exhibit 9. Quatramer – The Tumor Targeting Platform



Source: Hillstream BioPharma

**Intellectual Property:** Hillstream BioPharma has twenty-one issued patents and twenty-five pending U.S. patents. The patent expirations don't begin until 2036. In addition, Orphan Drug Designations have been granted for HSB-1216 and HSB-888.

**Valuation:** This is an early-stage company that is working now to establish proof of concept data. How should we value a company without proof-of-concept data in man? One fact that we consider is the current valuation – a market capitalization of just ~\$18M and an enterprise value of just ~\$10M. Hillstream has an early-stage oncology product platform that has the potential to be competitive in the billion-dollar-plus oncology markets. We assume clinical success and discount the results back to a net present value. To adjust for these and other associated risks, we apply a 30% risk cut in our therapeutic models, which is in addition to a 30% risk rate. The subsequent revenues are then fed into our income statement. To the income statement metrics, we then model a target valuation. We assume the company does raise additional capital, and as such, our valuation math includes projected changes in shares. Our valuation models: Free Cash Flow to the Firm (FCFF), discounted EPS (dEPS), and Sum-of-the-Parts (SOP), and as previously stated, use a 30% discount rate which is in addition to the therapeutic risk rate. We select 30% for micro-capitalized growth companies, and this represents our highest risk rate. The result of these three models is then equal-weighted and averaged and rounded to the nearest whole number to provide a 12-month target price.

### Exhibit 10. Free Cash Flow Model

DCF Valuation Using FCF (mln):

units ('000)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
EBIT	(8,757)	(7,702)	(4,815)	(4,863)	(4,912)	(8,000)	(3,000)	22,000	60,000	104,850	397,199	944,545
Tax Rate	0%	0%	0%	0%	0%	0%	0%	5%	10%	24%	33%	35%
EBIT(1-t)	(8,757)	(7,702)	(4,815)	(4,863)	(4,912)	(8,000)	(3,000)	20,900	54,000	79,896	264,852	613,577
CapEx												
Depreciation												
Change in NWC												
FCF	(8,757)	(7,702)	(4,815)	(4,863)	(4,912)	(8,000)	(3,000)	20,900	54,000	79,896	264,852	613,577
PV of FCF	(11,384)	(7,702)	(3,704)	(2,878)	(2,236)	(2,801)	(808)	4,330	8,606	9,794	24,975	44,508
Discount Rate	30%											
Long Term Growth Rate	1%											
Terminal Cash Flow	2,136,940											
Terminal Value YE2033	155,010											
NPV	215,711											
NPV-Debt	-											
Shares out (thousands)	68,661 2033E											
NPV Per Share	\$ 3.14											

Source: Dawson James estimates

### Exhibit 11. Discounted EPS Model

Current Year	2023
Year of EPS	2033
Earnings Multiple	10
Discount Factor	30%
Selected Year EPS	\$ 8.94
NPV	\$ 6.48

Source: Dawson James estimates

Discount Rate and Earnings Multiple Varies, Year is Constant							
2033 EPS							
Earnings Multiple	6.5	5%	10%	15%	20%	25%	30%
5		\$27.43	\$17.23	\$11.05	\$7.22	\$4.80	\$ 3.24
10		\$54.86	\$34.46	\$22.09	\$14.43	\$9.60	\$ 6.48
15		\$82.30	\$51.68	\$33.14	\$21.65	\$14.39	\$ 9.72
20		\$109.73	\$68.91	\$44.18	\$28.87	\$19.19	\$ 12.97
25		\$137.16	\$86.14	\$55.23	\$36.08	\$23.99	\$ 16.21
30		\$164.59	\$103.37	\$66.27	\$43.30	\$28.79	\$ 19.45
35		\$192.03	\$120.59	\$77.32	\$50.52	\$33.59	\$ 22.69
40		\$219.46	\$137.82	\$88.36	\$57.73	\$38.38	\$ 25.93

Source: Dawson James estimates

### Exhibit 12. Sum-of-the-Parts Model

Hillstream BioPharma	LT Gr	Discount Rate	Yrs. to Mkt Peak	% Success	Peak Sales MMs	Term Val
Cancer-1	1%	30%	8	70%	\$1,000	\$3,448
NPV						\$3.45
Cancer-2	1%	30%	10	70%	\$400	\$1,379
NPV						\$0.82
Net Margin						80%
MM Shrs OS (2030E)						69
Total						\$3.45

Source: Dawson James estimates

**Risks to our thesis include** 1. Regulatory Approvals; 2. Clinical Science 3. Adoption Rates 4. The competitive landscape 5. Intellectual Capital 6. Dilution

- **Regulatory Approvals.** The company's products require regulatory approvals, and there can be no assurances that the requirements to achieve these approvals can be met.
- **Clinical Science:** The company will need to demonstrate the products work.
- **Adoption Rates:** There are no assurances that the oncology products once developed will be competitive on the complex oncology landscape.
- **The Competitive Landscape & IP.** The company plans to operate in the highly competitive oncology landscape where well financed "bigpharma" dominates the field. The company does have intellectual property however there are no assurances that IP will not be challenged.
- **Dilution:** The company is likely to incur losses for the foreseeable future until it is able to generate sufficient revenue from product sales. Our model assumes a rising share count during this period. There can be no assurances that the company can successfully raise the capital required to execute its business strategy.

**Exhibit 13. Income Statement**

Hillstream BioPharma: Income Statement																
000 - YE December 31	2022E	1Q23E	2Q23E	3Q23E	4Q23E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
<b>Product sales</b>																
Product 1 - Oncology											10,000	50,000	100,000	160,000	350,000	700,000
Product 2 - Oncology															200,000	500,000
<b>Total Product Sales</b>	-	-	-	-	-	-	-	-	-	-	10,000	50,000	100,000	160,000	550,000	1,200,000
<b>Expenses</b>																
COGS											3,000	14,000	25,000	40,000	137,500	240,000
COGS %		0%	0%	0%	0%						30%	28%	25%	25%	25%	20%
Research and Development	2,445	704	734	734	763	2,934	3,521	4,225	6,500	5,200	5,252	5,777	6,933	8,319	9,983	11,980
General and Administrative	4,720	1,144	1,192	1,192	1,240	4,767	4,815	4,863	4,912	8,000	10,000	14,000	15,000	15,150	15,302	15,455
<b>Total Operating Expenses</b>	<b>7,166</b>	<b>1,848</b>	<b>1,925</b>	<b>1,925</b>	<b>2,002</b>	<b>7,702</b>	<b>4,815</b>	<b>4,863</b>	<b>4,912</b>	<b>8,000</b>	<b>13,000</b>	<b>28,000</b>	<b>40,000</b>	<b>55,150</b>	<b>152,802</b>	<b>255,455</b>
Loss from Operations	(7,166)	(1,848)	(1,925)	(1,925)	(2,002)	(7,702)	(4,815)	(4,863)	(4,912)	(8,000)	(3,000)	22,000	60,000	104,850	397,199	944,545
<b>Other Expense</b>																
Interest Expense	(1,591)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in Redemption Value																
<b>Total Other Expense</b>	<b>(1,591)</b>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<b>Net Loss</b>	<b>(8,757)</b>	<b>(1,848)</b>	<b>(1,925)</b>	<b>(1,925)</b>	<b>(2,002)</b>	<b>(7,702)</b>	<b>(4,815)</b>	<b>(4,863)</b>	<b>(4,912)</b>	<b>(8,000)</b>	<b>(3,000)</b>	<b>22,000</b>	<b>60,000</b>	<b>104,850</b>	<b>397,199</b>	<b>944,545</b>
												1,100	6,000	24,954	132,347	330,969
<b>Tax Rate</b>	<b>0%</b>	<b>5%</b>	<b>10%</b>	<b>24%</b>	<b>33%</b>	<b>35%</b>										
<b>GAAP Net Income (loss)</b>	<b>(8,757)</b>	<b>(1,848)</b>	<b>(1,925)</b>	<b>(1,925)</b>	<b>(2,002)</b>	<b>(7,702)</b>	<b>(4,815)</b>	<b>(4,863)</b>	<b>(4,912)</b>	<b>(8,000)</b>	<b>(3,000)</b>	<b>20,900</b>	<b>54,000</b>	<b>79,896</b>	<b>264,852</b>	<b>613,577</b>
<b>GAAP-EPS</b>	<b>(0.78)</b>	<b>(0.15)</b>	<b>(0.16)</b>	<b>(0.07)</b>	<b>(0.07)</b>	<b>(0.46)</b>	<b>(0.17)</b>	<b>(0.12)</b>	<b>(0.07)</b>	<b>(0.09)</b>	<b>(0.03)</b>	<b>0.21</b>	<b>0.52</b>	<b>0.74</b>	<b>4.01</b>	<b>8.94</b>
GAAP EPS (dil)	(0.77)	(0.15)	(0.16)	(0.06)	(0.06)	(0.35)	(0.11)	(0.09)	(0.05)	(0.06)	(0.02)	0.14	0.35	0.74	4.01	8.94
Wgtd Avg Shrs (Bas) '000	11,306	12,005	12,125	27,246	27,519	19,724	35,264	43,392	73,095	87,229	95,897	99,791	103,842	108,059	65,982	68,661
Wgtd Avg Shrs (Dil) '000	11,306	12,005	12,125	32,246	32,569	22,236	42,865	53,608	93,876	128,141	141,033	146,760	152,719	158,920	65,982	68,661

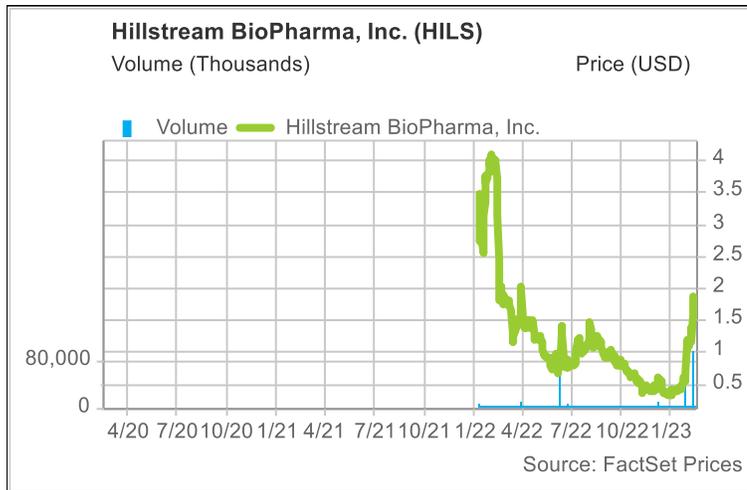
Source: Company reports and Dawson James

Source: Dawson James estimates, company reports

Companies mentioned in this report:

**Important Disclosures:**

**Price Chart:**



Price target and ratings changes over the past three years:

Initiated – Buy – February 22, 2023 – Price Target \$4.0

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Current as of 22-Feb-23

	<b>Company Coverage</b>		<b>Investment Banking</b>	
<b>Ratings Distribution</b>	# of Companies	% of Total	# of Companies	% of Totals
Market Outperform (Buy)	23	68%	1	4%
Market Perform (Neutral)	11	32%	2	18%
Market Underperform (Sell)	0	0%	0	0%
<b>Total</b>	<b>34</b>	<b>100%</b>	<b>3</b>	<b>9%</b>

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