Valuation and Clinical Pipeline Analysis of Leap Therapeutics (LPTX)

Executive Summary

Leap Therapeutics (NASDAQ: LPTX) is a clinical-stage biotech focused on targeted immuno-oncology therapies for gastrointestinal and solid tumors. The company has two main clinical-stage assets:

- **Sirexatamab (DKN-01)**: An anti-DKK1 monoclonal antibody in Phase 2 trials for gastric, colorectal, and endometrial cancers. Notable efficacy includes a 73% ORR in gastric/GEJ cancer and 90% ORR in DKK1-high tumors.
- **FL-301**: An anti-Claudin18.2 antibody, validated by the success of zolbetuximab in gastric cancer. Currently in Phase 1/2a.

Despite promising clinical data, Leap trades at a market cap of ~$15 million, below its $32.7M in cash. This reflects dilution concerns and investor skepticism. With a fully diluted share count of ~50 million, Leap has considerable upside in positive readout scenarios.

Recent peer deals include:

- **Amgen's $1.9B acquisition of Five Prime**
- **Astellas' $1.4B acquisition of Ganymed**

Leap could see a similar revaluation or acquisition if trials succeed.

Pipeline Overview

Drug (Target)	Indications (Status)	Phase	Key Notes
Sirexatamab (DKN-01)anti-DKK1	Gastric/GEJ (1L, Phase 2),Colorectal (2L, Phase 2),Endometrial (Phase 2 IST)	Phase 2	Trials: DisTinGuish, DeFianCe; biomarker-driven (DKK1-high); strong early efficacy data.
FL-301anti-Claudin18.2	Gastric/GEJ, Pancreatic, Claudin18.2+ solid tumors	Phase 1/2a	Inherited via Flame Biosciences merger. Validated target. Early-stage.
FL-302 Claudin18.2 x CD137 bispecific	Preclinical	IND-enabling	Immune co-stimulation strategy.
FL-501anti-GDF15	Preclinical	Pre-IND	Cancer cachexia and immune evasion target.

Clinical Program Summaries

Sirexatamab (DKN-01)

- **Mechanism**: Blocks DKK1, reducing immune suppression and tumor angiogenesis.
- **Gastric/GEJ (DisTinGuish Trial)**: ORR 73% overall, 90% in DKK1-high; PFS ~11.3 months.
- **Colorectal (DeFianCe Trial)**: 35% ORR in MSS CRC vs historical 5–13%.
- **Endometrial**: Early data shows CRs and DCR improvement in DKK1-high tumors; combination with pembrolizumab underway.

FL-301 (Anti-Claudin18.2)

- **Mechanism**: Targets CLDN18.2, tumor-specific tight junction protein.
- **Validation**: Zolbetuximab success in gastric cancer confirms viability.
- **Phase 1/2a**: Dose escalation ongoing; expansion into pancreatic, gastric/GEJ, and exploratory tumors planned.
- **Differentiators**: Fully human design; exploratory use in lung and ovarian cancer.

Market Opportunity Estimates

- **Gastric/GEJ Cancer**: Global therapy market ~$6.7B in 2023; DKN-01 could target 15–20k patients/year with peak sales in the hundreds of millions.
- **Colorectal Cancer**: ~145k new US cases/year; second-line MSS CRC is a large unmet need.
- **Endometrial Cancer**: Niche use in recurrent Wnt-mutant tumors.
- **Pancreatic Cancer**: >60% CLDN18.2-positive; potential for FL-301 to address this high-mortality cancer.

Financial Overview

Metric	Value (as of Q1 2025)
Cash on Hand	$32.7M
Market Cap	~$15M
Shares Outstanding	38.33M
Fully Diluted Shares	~50M

- **Dilution Risks**: Several legacy and low-priced warrants; options outstanding; past toxic financings.
- **Cost Control**: 50% workforce cut in May 2025 to preserve cash.

Valuation Scenarios

1. Optimistic

- **Assumptions**: Positive Phase 2 readouts in gastric & CRC; FL-301 shows early activity.
- **Valuation**: EV of ~$500M–$1B+; ~$10/share (50M FD shares).

2. Base Case

- **Assumptions**: Mixed Phase 2 data; some benefit in subgroups; funding needed.
- **Valuation**: EV of ~$100–150M; ~$2–3/share.

3. Pessimistic

- **Assumptions**: Trials fail or show no meaningful advantage.
- **Valuation**: EV ~$0–$20M; cash value; ~$0.20/share or lower.

Acquisition Potential

- **Past Comps**:
    - Five Prime (FGFR2b): $1.9B by Amgen
    - Ganymed (CLDN18.2): $1.4B by Astellas
- **Leap Buyout Estimate**:
    - Optimistic: $750M–$1B
    - Base: $200–300M
    - Pessimistic: Near cash (~$20–30M)

Conclusion

Leap Therapeutics offers a binary risk-reward profile. Despite its low valuation, it has:

- A strong clinical rationale for two immuno-oncology antibodies.
- Encouraging early data, particularly in biomarker-selected populations.
- Strategic potential for partnerships or acquisition.

If upcoming Phase 2 trials succeed, the stock could appreciate dramatically from current levels. Conversely, trial failure or poor data could limit value to cash on hand or force a pivot. The next 12–18 months are pivotal for Leap's valuation trajectory.

Sources: leaptx.com, pubmed.ncbi.nlm.nih.gov, biospace.com, aging.networkofcare.org, investors.leaptx.com, marketscreener.com, sec.gov, fiercebiotech.com, pharmacytimes.com, drugpatentwatch.com, mordorintelligence.com.