



**LLS TAP**

# THERAPY ACCELERATION PROGRAM

LORE GRUENBAUM, VP, TAP  
JAVEED FROOZAN, VP, BD & SA

July 2022



LEUKEMIA &  
LYMPHOMA  
SOCIETY®

# LLS MISSION AND PURPOSE

The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

We fund **RESEARCH** to advance lifesaving treatments.

We provide patients, survivors, caregivers, families and healthcare professionals with hope, guidance, **EDUCATION** and **SUPPORT**.

We drive **ADVOCACY** for policies that protect patient access to lifesaving treatment.



Approximately every **3 minutes** someone in the U.S. is diagnosed with blood cancer



Nearly **1.4 million** people in the U.S. are living with or in remission from leukemia, lymphoma or myeloma

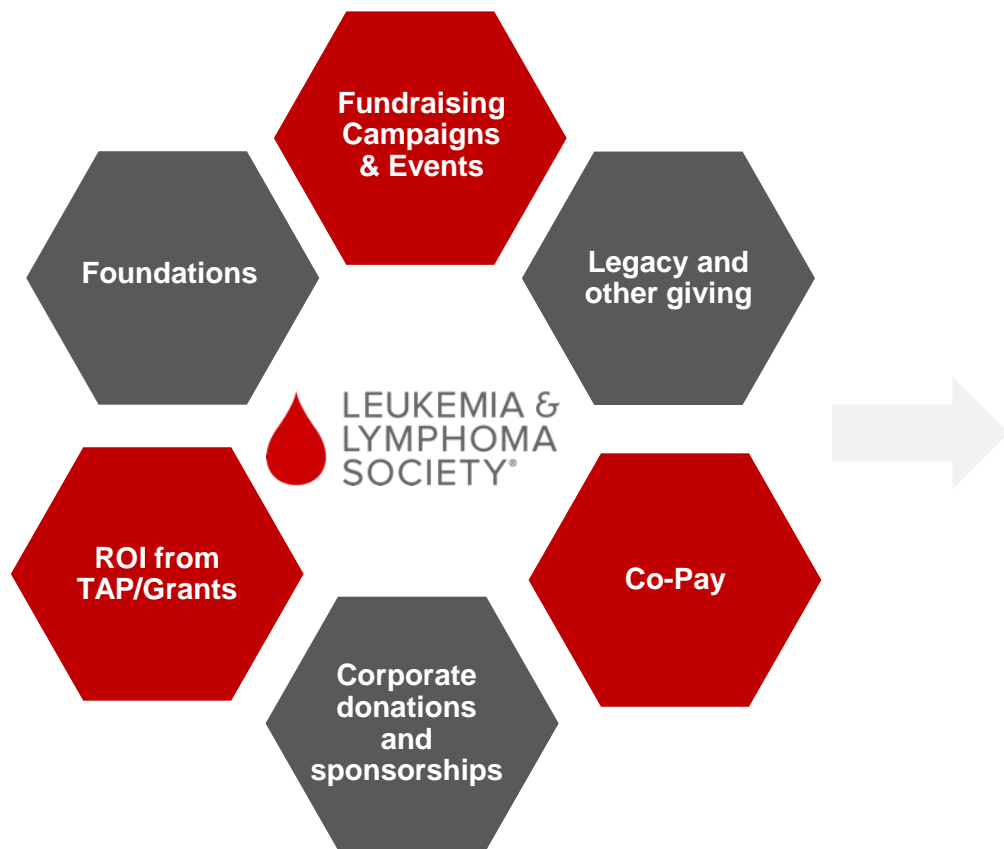


About **30 percent** of blood cancer patients still do not survive five years after diagnosis



About **40 percent** of all pediatric cancers are blood cancers

# LLS MISSION INVESTMENT IS SUPPORTED BY MULTIPLE REVENUE SOURCES

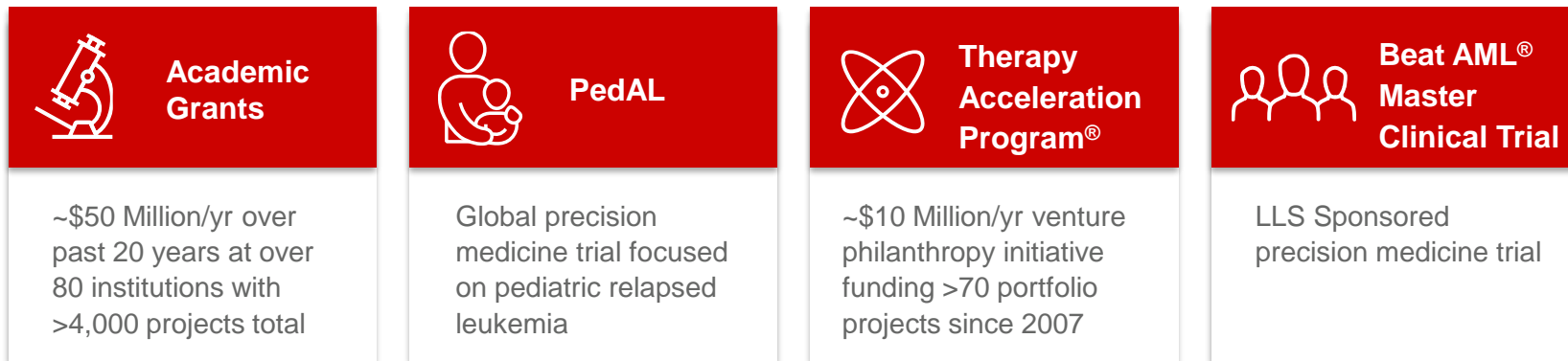
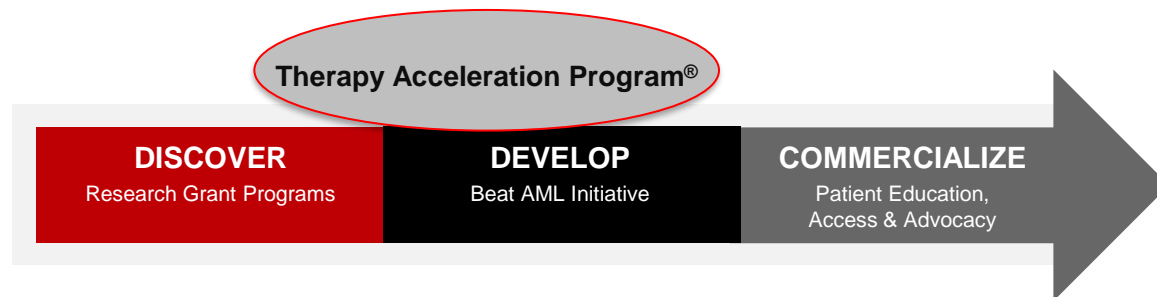


## OUR IMPACT

- Invested nearly \$1.3 billion in research and development worldwide since founded in 1949
- Helped advance 52 of 60 FDA approved blood cancer drugs
- Supported >93,000 patients since inception
- Responded to 20,000 inquiries in 2019

# LLS GLOBAL RESEARCH AND DEVELOPMENT FOCUS

Research and development programs and clinical trials using LLS resources



# LLS THERAPY ACCELERATION PROGRAM (TAP)

## Venture philanthropy funding to support novel therapies

Established in 2007

>\$130 Million invested to date

- Biotech: >\$95 Million
- Institutions: ~\$35 Million
- >70 financings of companies and assets
- >20 assets currently in active development

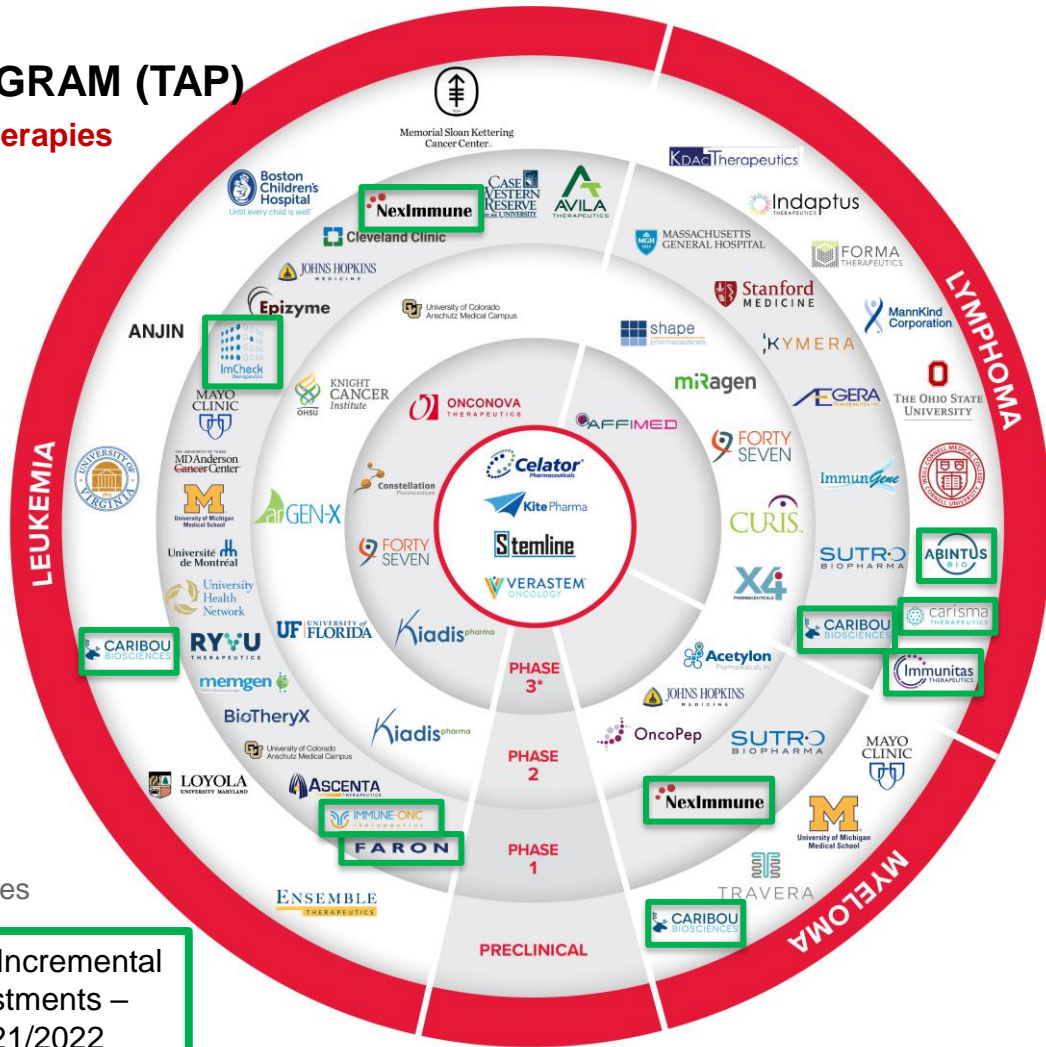
### 4 Approved Therapies to Benefit Patients

- Vyxeos (AML) - FDA
- Yescarta (DLBCL, tFL, PMBCL) - FDA
- Elzonris (BPDCN) - FDA
- Copiktra (PTCL) - NCCN

### ROI Focus:

- FDA Approvals
- Assets in clinical development
- Strategic transactions & financing for portfolio companies
- Financial ROI to LLS

New + Incremental  
Investments –  
2021/2022



\*Includes Phase 2 registration-enabling studies

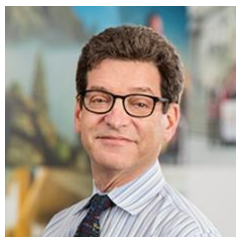


# LLS TAP SCIENTIFIC & BUSINESS LEADERSHIP



**Lore Gruenbaum, PhD**  
VP, TAP

- 20 years drug discovery & clinical development
- VP, Gotham Therapeutics; Exec Dir, Applied Biomath
- Biomarker Head, Virology, Roche; Group Leader, BI
- Yale postdoctoral work, principal investigator and collaborator on several SBIR grants



**Lee Greenberger, PhD**  
SVP, Chief Scientific Officer

- 20 years big pharma and biotech
- Oversight responsibility for >\$50 M annual research budget
- Advanced > 10 oncology therapeutics into the clinic
- Search & due diligence experience with big pharma



**Javeed Froozan, MBA, BS**  
VP, Business Development

- 25 years biopharma and health technology value creation
- Sr. Dir, Emergent BioSolutions, Multiple start-ups/exits, 2 IPOs
- Business lead on EBS-Trubion M&A transaction. Alliance Manager for Pfizer relationship
- Strategic Investments, M&A, Business Development, Asset Management, and Economic Development



**Blaine Robinson, PhD**  
Executive Director, TAP

- 15 years research & clinical development in blood cancer
- Search & Diligence on 100+ projects
- Scientific lead for over 20 TAP projects including Constellation, Kymera, Ryvu & most recently Abintus, Caribou & Immune-Onc
- Pediatric leukemia researcher, Children's Hospital of Philadelphia



**Jun Xu, PhD**  
Executive Director – TAP Lead

- 20 years oncology/immunology drug discovery/development
- Search & Diligence on 100+ projects
- Scientific lead for over 20 TAP projects including multiple high impact ones, such as Stemline, Kite, argenX, Forty Seven & most recently Carisma

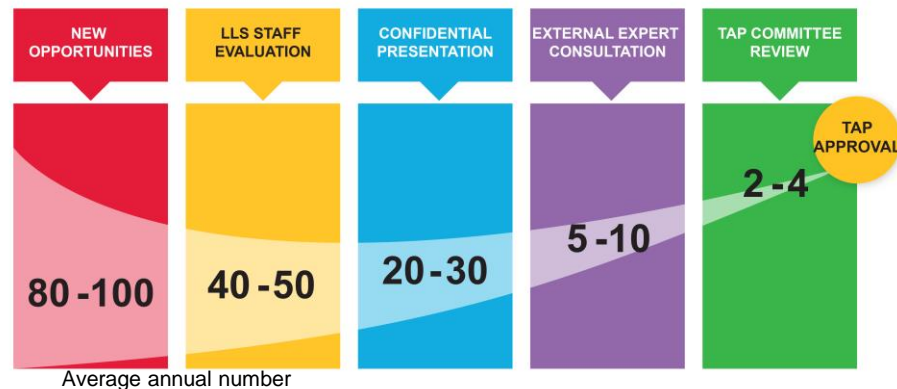
**Therapy Acceleration Program Committee:** <https://www.lls.org/therapy-acceleration-program/oversight>

# TAP GOALS & INVESTMENT STRATEGY

Accelerate innovative blood cancer therapies and generate ROI for LLS mission

## Focus on high-value assets:

- Existing and emerging populations with high unmet needs
- Gaps in current and emerging treatment landscape
- Innovative science, first-in-class assets
- First-in-heme/onc and registration trials
- Strong intellectual property, management, and finances



## 2 PATHS TO CO-INVEST WITH INVESTORS AND VENTURE PHILANTHROPIES



### Strategic

- Range of Investment: \$2 Million to \$10 Million
- Presentation to TAP Committee
- Typically, 3-6 months to reach TAP Committee



### Opportunistic

- Target Investment: \$500,000
- LLS TAP team briefs TAP Committee Chair
- Transaction completion in 1-3 months



# TAP ACTIVELY COLLABORATES WITH PARTNER COMPANIES

## Investment Side Letter & Research Advisory Committee

### Key features of LLS TAP Investment Side Letter

- Cites LLS Mission focus and company's focus and assets in blood cancer
- Investment amount on same terms and conditions as other investors, and use of proceeds (less detail for public companies)
- Exclusion of fees on LLS proceeds to investment banks and other intermediaries (via waiver, decreased total load, or refund to company)
- Information & observer rights (private firms)
- Research Advisory Committee (RAC) structure for recurring meetings between TAP team and company to discuss corporate and program progress – Company retains control of program
- Company participation in LLS events, publication review, and evaluate providing research materials to PI's.

**Side letter captures the mission-driven collaborative nature of the relationship between LLS TAP and the partner companies**



# TAP VALUE ADD TO BIOTECH COMPANIES

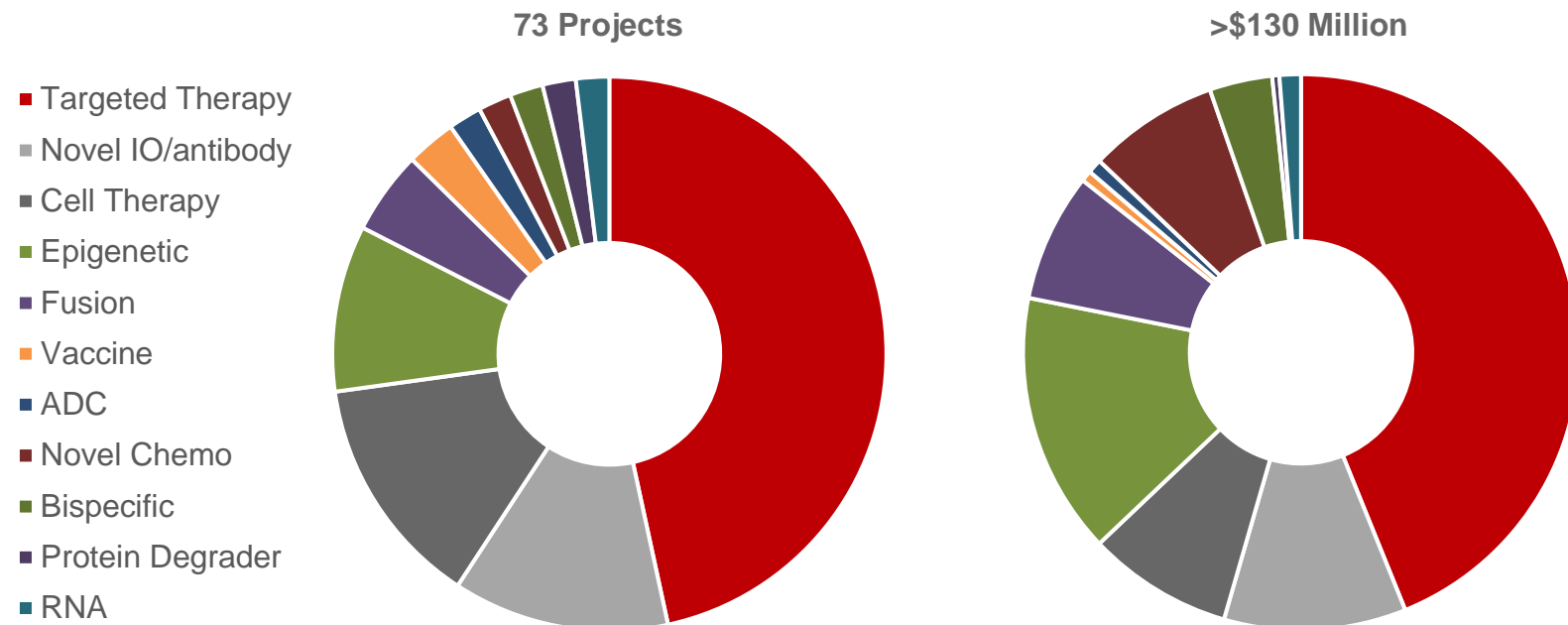
**TAP-funded companies benefit from LLS blood cancer insight**

- Deep knowledge of indications and rapidly changing SoC
- Unique scientific, clinical, and drug development expertise
- Patient access services to enable understanding of patient needs
- Immediate access to extensive KOL network
- Pharmaceutical, biotech, and research institution partner connections
- Regulatory insight through LLS initiatives (Beat AML Master Clinical Trial®)

**TAP record of success provides scientific & investment credibility, and visibility enabling companies to raise additional funds.**

# TAP PORTFOLIO THERAPEUTIC PLATFORMS FUNDED (2007-2022)

Portfolio is aligned with strong industry focus on Targeted Therapy and reflects growing interest in Cell and IO Therapies in blood cancer





# TAP PORTFOLIO ASSETS IN DEVELOPMENT

Therapy	Target/Modality	Indications	Preclinical	Phase 1	Phase 2	Phase 2 Reg / Phase 3	Regulatory Status
Magrolimab + Azacitidine	CD47 antibody	MDS				FortySeven <sup>1</sup>	
AFM13	CD30/CD16A bispecific engager	PTCL				AFFIMED <sup>1</sup>	
Pelabresib + Ruxolitinib	BET small molecule	MPN				Constellation <sup>2</sup> PHARMACEUTICALS	
Magrolimab + Rituximab	CD47 antibody	DLBCL			FortySeven <sup>1</sup>		
Cusatuzumab + Azacitidine	CD70 antibody	AML			argenx		
Ziftomenib	Menin small molecule	AML: NPM1 mutant & KMT2A rearranged		KURA <sup>3</sup> ONCOLOGY			
STRO-001	CD74 antibody drug conjugate	NHL/MM		SUTRO BIOPHARMA			
Mavoxiafor + Ibrutinib	CXCR4 small molecule	CXCR4 & MYD88 double mutant Waldenström's		X4 PHARMACEUTICALS			
IO-202	LILRB4 antibody	AML/CMML		IMMUNE-ONC THERAPEUTICS			
RVU120	CDK8/19 small molecule	AML/MDS		RYU THERAPEUTICS			
ICT01	BTN3A antibody	heme malignancies		ImCheck therapeutics			
PVX-410 + ACY-241 +/- Len	XBP1/CD138/CS1 vaccine	Smoldering myeloma		OncoPep			
NEXI-001	T cell therapy	AML		NexImmune			
NEXI-002	T cell therapy	MM		NexImmune			
BTX-1188	GSPT1 + IKZF1/3 degrader	AML/NHL		biotheryx			
CB-010	CD19/PD1 KO allogeneic CAR	NHL		CARIBOU BIOSCIENCES			
KT-333	STAT3 degrader	PTCL/CTCL/LGL-L		KYMERA			
KT-413	IRAK1MiD degrader	MYD88 mutant DLBCL		KYMERA			
Bexmarilimab	Cleaver-1 antibody	AML/MDS		FARON			
IMT-009	CD161 antibody	NHL	Immunitas THERAPEUTICS				
TBD	<i>in vivo</i> CAR-X	TBD	ABINTUS				
TBD	CAR macrophage	TBD	carisma THERAPEUTICS				

	Orphan Drug Designation
	Fast Track Designation
	Breakthrough Therapy Designation

Updated July 2022

LEUKEMIA & LYMPHOMA SOCIETY®

# TAP FUNDED ASSETS CREATE VALUE

TAP portfolio partners have had successful M&A, collaboration and licensing transactions

	➔	
 		
		
		
		
		
		
		
		
		
		

Transactions  
>\$20 Billion



## TAP PORTFOLIO COMPANY WITH ASSETS IN ACTIVE BLOOD CANCER DEVELOPMENT

# SIGNIFICANT EQUITY FINANCING RAISED CONCURRENT WITH OR POST- LLS TAP FUNDING

Equity since TAP Funding*	TAP Portfolio Company
>\$1 Billion	argenx Epizyme
>\$500 Million	Constellation <sup>1</sup> Kura <sup>2</sup> Kymera <sup>2</sup>
\$250-\$500 Million	Caribou <sup>2</sup> Curis Forty Seven <sup>3</sup> Sutro
\$100-\$250 Million	Affimed BioTheryx <sup>2</sup> ImCheck <sup>2</sup> Neximmune <sup>2</sup> X4 <sup>2</sup>
\$50-\$100 Million	Carisma <sup>2</sup> Immune-Onc <sup>2</sup> Immunitas <sup>2</sup> Ryvu WindMIL <sup>2</sup>
<\$50 Million	Abintus <sup>2</sup> Faron <sup>2</sup> Indaptus <sup>2</sup> OncoPep <sup>2</sup>

1: LLS asset funding (07/2021 M&A by MorphoSys); 2: LLS equity;  
3: LLS equity participation plus asset funding (05/2020 M&A by Gilead)



# KEY POINTS

## LLS TAP has established record of success

- Targeting unmet medical needs
- Leading to FDA approvals of life changing therapeutics
- Creating value for patients, companies and ROI for the LLS mission

## LLS would like to expand the reach & impact of the TAP program

- Leverage its unique expertise in novel collaborations
- Attract more companies and investors to blood cancer indications
- Expand TAP capacity to support the most promising assets

## For more information, contact:

Lore Gruenbaum, PhD 914.821.8361 | [Lore.Gruenbaum@LLS.org](mailto:Lore.Gruenbaum@LLS.org)

Javeed Froozan, MBA 914.821.8817 | [Javeed.Froozan@LLS.org](mailto:Javeed.Froozan@LLS.org)

# **TAP SUCCESS STORIES**

# TAP SUCCESS: NOVEL LIPOSOMAL CYTOTOXIC THERAPY

Vyxeos® is the first FDA-approved treatment for two types of poor-prognosis AML (2017)

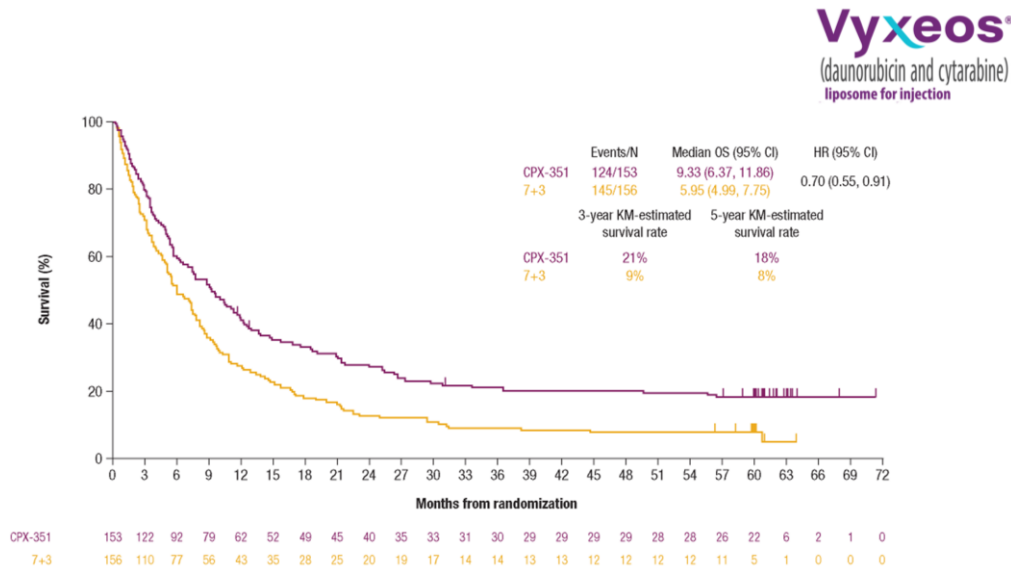


**ACQUIRED BY JAZZ PHARMA  
FOR \$1.5 BILLION IN 2016**

**LLS TAP PROVIDED:**

**\$9.15 MILLION ASSET FUNDING**

**ROI: \$25.3 MILLION**



Five-year final results of a phase 3 study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML

*J. Lancet et al., ASCO 2020*

# TAP SUCCESS: CD19 CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY

**Yescarta® is the first FDA-approved CAR-T Therapy in NHL (2017)**

**LLS has invested > \$80 M in Cellular Immunotherapy since 1998**

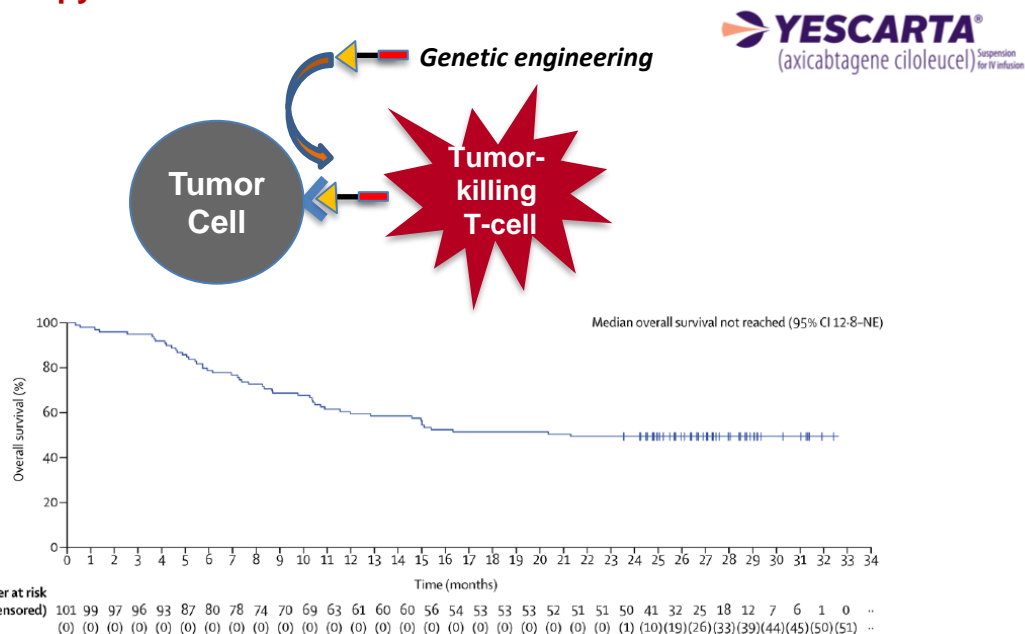


**ACQUIRED BY GILEAD  
FOR \$11.9 BILLION IN 2017**

**LLS TAP PROVIDED:**

**\$2.5 MILLION ASSET FUNDING**

**ROI: \$6.25 MILLION**



Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicenter, Ph 1-2 trial

*Locke et al. 2019. Lancet Oncology*

# TAP SUCCESS: NOVEL TARGETED CD123 FUSION PROTEIN

**Elzonris® is the first approved therapy for rare blood cancer indication BPDCN (2018)**

**Stemline**

acquired by  **MENARINI**  
group

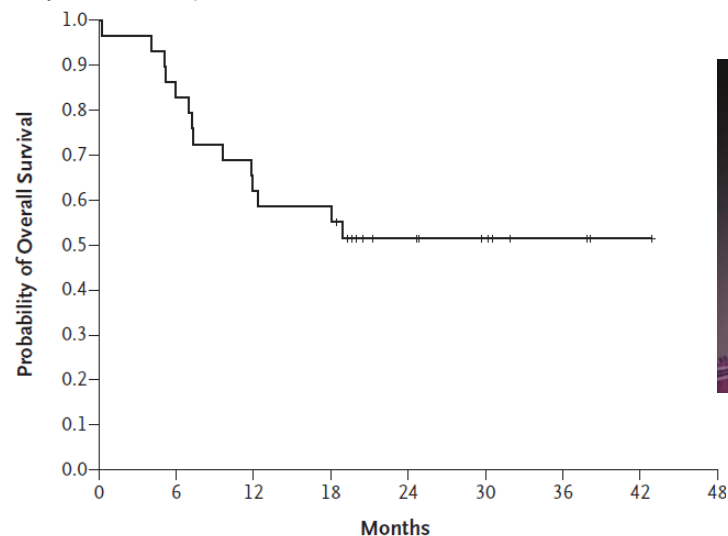
**ACQUIRED BY MENARINI GROUP  
FOR \$677 MILLION IN 2020**

**LLS TAP PROVIDED:**

**\$2.9 MILLION NET ASSET FUNDING**

**ROI: \$7.25 MILLION TO DATE**

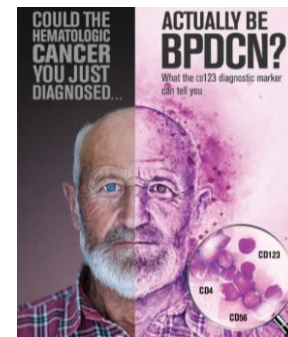
**B Kaplan–Meier Analysis of Overall Survival**



Treatment outcomes of 29 patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN) who received first-line treatment with tagraxofusp: Probability of overall survival

*Pemmaraju et al., 2019. NEM*

 **ELZONRIS®**  
(tagraxofusp-erzs) injection





# TAP SUCCESS: DUVELISIB (DUAL PI3K INHIBITOR)

**Copiktra® is the first dual PI3K inhibitor included in NCCN Guidelines for all subtypes of PTCL (2021)**



duvelisib acquired by  
SECURA BIO™

**LICENSED TO SECURA BIO  
FOR UP TO \$311 MILLION IN 2020**

**LLS TAP PROVIDED:**

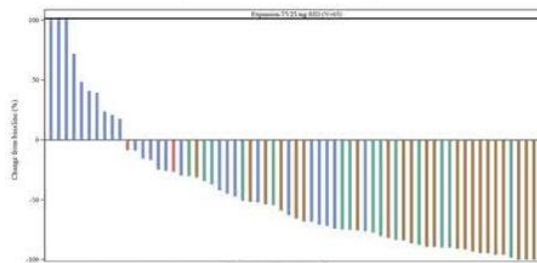
**\$1.485 MILLION ASSET FUNDING**

**ROI: TBD**



## Dose Expansion: Results

Best percent change from baseline in target lesions (n=65)\*



\*65 out of 78 subjects had both best overall response (CR, PR, SD, PD) and data available to compute percent change from baseline sum of target lesions

Number of patients dosed	78
Summary of responses, by IRC	39(50)
Number of Responders (Lugano Criteria), n (%)	
CR	25(32.1)
PR	14(17.9)
Duration of response in days	233
Median (95% CI)	(90, NC)
Range	(1+, 420+)
Number of patients discontinued from treatment n, (%)	64 (82.1)
Disease progression	34(43.6)
Death	4(5.1)
Transplant	5(6.4)
Adverse Event	14(17.9)
Other	7(8.9)
Median time to response, days (range)	53(15,114)
Number of patients continued on treatment n(%)	14(18)
Minimum follow up, months	6

*Brammer et al., ASH 2021*

- "Patients with r/r PTCL usually relapse quickly and have limited treatment options, and the data from the PRIMO trial show very promising activity and even a remarkable number of complete responses. Importantly, these responses are better than current standard of care options" said Dr. Brammer.



# TAP SUCCESS: MAGROLIMAB (ANTI-CD47 ANTIBODY)

**Magrolimab + Azacitidine induces high response rates in MDS and AML**

**Initiation of registration-enabling studies in 2020**

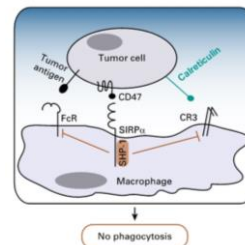


**ACQUIRED BY GILEAD  
FOR \$4.9 BILLION IN 2020**

**LLS TAP PROVIDED:**

**\$4.175 MILLION ASSET FUNDING  
\$3 MILLION EQUITY INVESTMENT**

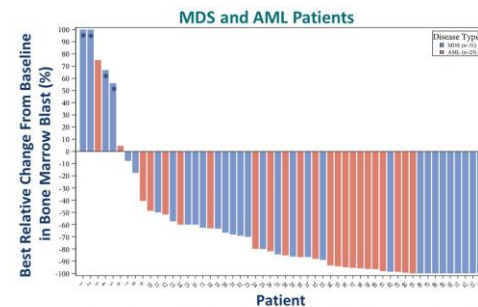
**ROI: >\$40 MILLION**



Magrolimab blocks the 'don't eat me' signal on tumor cells

Best Overall Response	1L MDS N=33	1L AML N=25
ORR	30 (91%)	16 (64%)
CR	14 (42%)	10 (40%)
CRi	NA	4 (16%)
PR	1 (3%)	1 (4%)
MLFS/marrow CR	8 (24%) 4 with marrow CR + HI	1 (4%)
Hematologic improvement (HI)	7 (21%)	NA
SD	3 (9%)	8 (32%)
PD	0	1 (4%)

Response assessments per 2008 IWG MDS criteria and 2017 AML ELN criteria. Patients with at least 1 post-treatment response assessment are shown; all other patients are on therapy and are too early for first response assessment, except for 2 MDS patients not evaluable (withdrawal of consent) and 3 AML patients (1 AE, 2 early withdrawal).



Four patients not shown due to missing values; <5% blasts imputed as 2.5%. \*Baseline bone marrow blasts ≤5%.

- Magrolimab + AZA induces a 91% ORR (42% CR) in MDS and 64% ORR (56% CR/CRi) in AML
- Responses deepened over time with a 56% 6-month CR rate in MDS patients (assessed in all patients 6 months after initial treatment)
- Median time to response is 1.9 months, more rapid than AZA alone
- Magrolimab + AZA efficacy compares favorably to AZA monotherapy (CR rate 6-17%<sup>1,2</sup>)

1. Azacitidine USPL. 2. Fenaux P, et al. *Lancet Oncol*. 2009;10(3):223-232.

PRESENTED AT: **2020 ASCO ANNUAL MEETING**

#ASCO20  
ORAL AND POSTER PRESENTATIONS

PRESENTED BY: DAVID A. SALLMAN, MD

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# TAP SUCCESS: KO-539 (MENIN INHIBITOR)

First-in-class inhibitor of the menin-MLL interaction in Ph1 trial for patients with relapsed/refractory AML



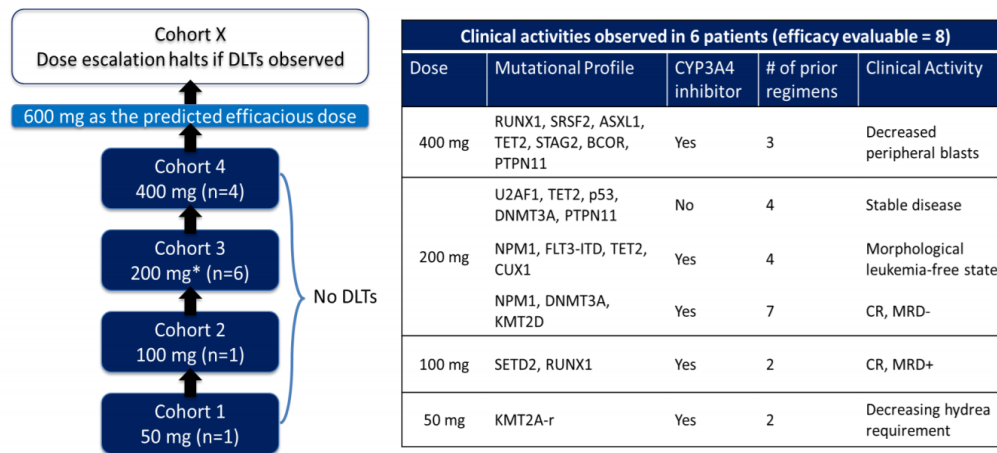
**PRECLINICAL COMPOUNDS  
RELATED TO KO-539 LICENSED  
TO KURA ONCOLOGY IN 2015**

**LLS TAP PROVIDED:**

**\$6.31 MILLION ASSET FUNDING  
TO U MICHIGAN**

**ROI: EQUITY: 26,000+ SHARES  
+ \$26,000+ CASH TO DATE**

## KO-539 Demonstrates Encouraging Early Clinical Activity



\*Expanded to characterize PK

Data as of 02 November 2020



American Society of Hematology

Wang et al. ASH 2020 #115

- Grants initially and then TAP supported preclinical development (including chemistry) of menin-MLL interaction inhibitors by Jolanta Grembecka at University of Michigan and licensing of assets to Kura Oncology in Dec 2014
- Phase 1/2a trial for R/R AML with MLL fusions/NPM1 mutations
  - First patient dosed in Sept 2019
  - Initiated expansion cohorts in July 2021



# TAP SUCCESS: PELABRESIB (BET INHIBITOR)

**Pelabrelib + Ruxolitinib induces high spleen volume response rates in JAK-naïve myelofibrosis**

**Initiation of registration-enabling study in 2020**

**First Novel Mechanism Beyond JAK Inhibitors to Demonstrate POC in 1L MF**



**ACQUIRED BY MORPHOSYS  
FOR \$1.7 BILLION IN 2021**

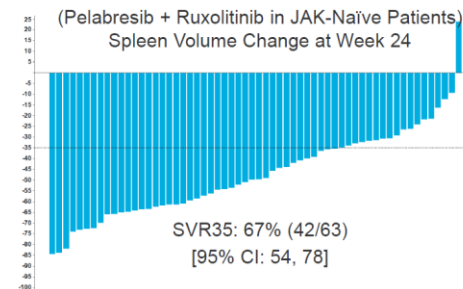
**LLS TAP PROVIDED:**

**\$7.35 MILLION ASSET FUNDING**

**ROI: \$7.35 MILLION TO DATE**

- Robust response rate to date in trial of > 60 1L patients
- Strong activity observed as a monotherapy and add on to ruxolitinib 2L+ patients
- Translational data and improvement in anemia supports disease-modifying potential
- Pelabresib has been generally well-tolerated to date
- Phase 3 trial (MANIFEST-2) under way

Data cutoff September 29, 2020 of MANIFEST trial  
SVR35 = ≥35% spleen volume reduction from baseline



	1L setting (Arm 3)			
	Upfront combo with ruxolitinib	COMFORT-1*	COMFORT-2**	SIMPLIFY-1***
24-Week SVR35 Rate	67% (42/63)	41.9%	32%	29%

SVR35 response = ≥35% spleen volume reduction (Measured at 24 Weeks)

\* COMFORT-1: A Double-blind, Placebo-controlled Trial of ruxolitinib for Myelofibrosis. Verstovsek, S., et al; N Engl J Med 2012;366:799-807.

\*\* COMFORT-2: A Double-blind, Placebo-controlled Trial of ruxolitinib vs. Best Available Therapy (BAT) for Myelofibrosis. Harrison, C., et al; NEJM 2012; 336: 787-798.

\*\*\* SIMPLIFY-1: A Phase III Randomized Trial of Mometinib Versus ruxolitinib in Janus Kinase Inhibitor-Naïve Patients With Myelofibrosis. Mesa, R., et al. J Clin Oncol 2017; 35(34):3844-3850.

# THERAPY ACCELERATION PROGRAM COMMITTEE

**Casey Cunningham, MD (Chair) +**  
Santé Ventures

**Stephen Ansell, MD, PhD**  
Mayo Clinic Rochester

**Madhav Dhodapkar, MBBS**  
Emory University

**Courtney DiNardo, MD**  
The University of Texas MD Anderson Cancer Center

**Giulio Draetta, MD, PhD**  
The University of Texas MD Anderson Cancer Center

**Christopher Flowers, MD +**  
The University of Texas MD Anderson Cancer Center

**Patrick Fortune, PhD, MBA**  
Partners Healthcare Systems

**Tapan Kadia, MD**  
The University of Texas MD Anderson Cancer Center

**Laura Kaufman, PhD, DABT**  
Private Consultant

**Ronald Levy, MD**  
Stanford University School of Medicine

**Fred Locke, MD**  
Moffitt Cancer Center

**Ruben Mesa, MD +**  
UT Health San Antonio

**Vern Norviel, JD**  
Wilson Sonsini Goodrich & Rosati

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University of Colorado

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Grewhawke Capital Advisors

**Steven Rosen, MD**  
City of Hope

**Robert Spiegel, MD**  
Spiegel Consulting LLC

**Keith Stewart, MD**  
Princess Margaret Cancer Center

# THANK YOU!

## LLS Research Grants and TAP



**Lee Greenberger, PhD**  
*CSO & SVP Research*



**Michael Yaffe, PhD**  
*VP of Research*



**Erik Nelson, PhD**  
*Exec. Dir. Research*



**James Kasper, MS**  
*Exec. Dir. Research*



**Orsi Giricz, PhD**  
*Dir. Research*



**Lore Gruenbaum, PhD**  
*VP of TAP*



**Jun Xu, PhD**  
*Exec. Dir. TAP Lead*



**Blaine Robinson, PhD**  
*Exec. Dir. TAP*



**Javeed Froozan, MBA**  
*VP of BD & Alliance*