



LLS TAP

THERAPY ACCELERATION PROGRAM

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

October 2021

BEATING CANCER IS IN OUR BLOOD.



LEUKEMIA &
LYMPHOMA
SOCIETY®

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



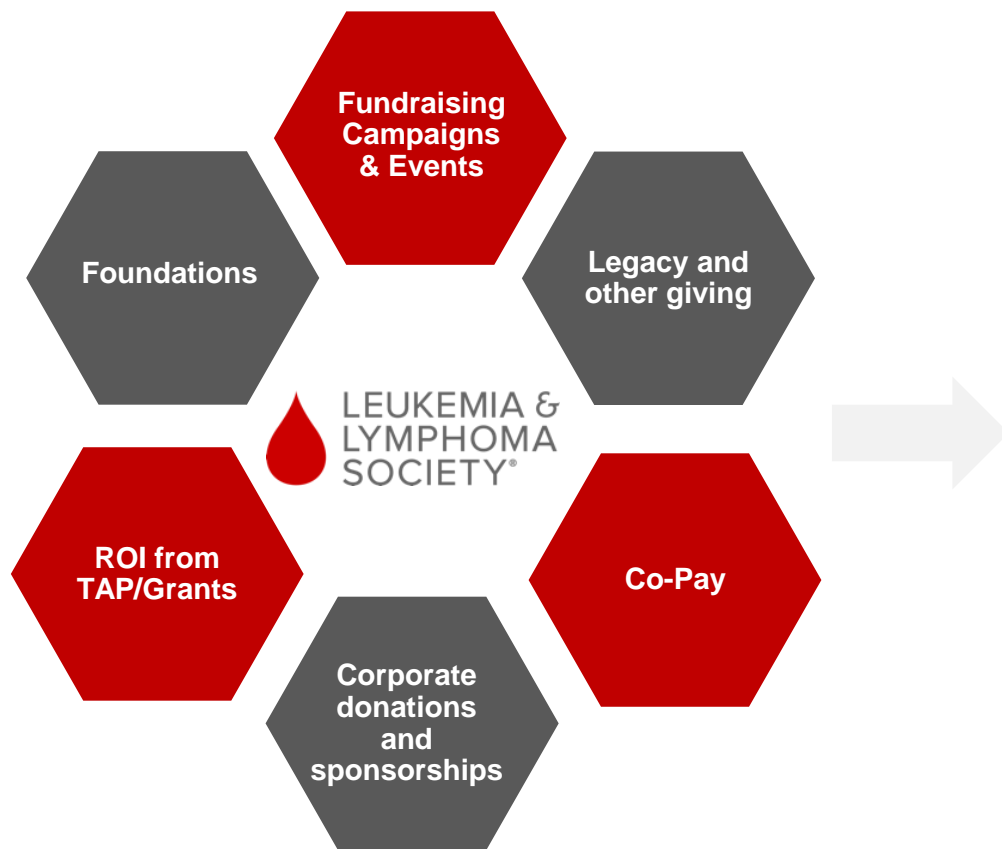
Nearly **1.4 million** people in the U.S. are living with or in remission from leukemia, lymphoma or myeloma



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


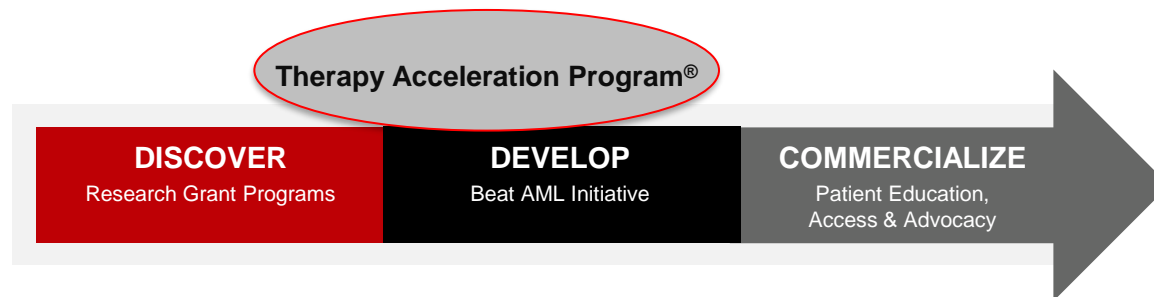


OUR IMPACT

- 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



Academic Grants

~\$50 Million/yr over past 20 years at over 80 institutions with >4,000 projects total



PedAL

Global precision medicine trial focused on pediatric relapsed leukemia



Therapy Acceleration Program®

~\$10 Million/yr venture philanthropy initiative funding >70 portfolio projects since 2007



Beat AML® Master Clinical Trial

LLS Sponsored precision medicine trial

LLS THERAPY ACCELERATION PROGRAM (TAP)

Venture philanthropy funding to support novel therapies

Established in 2007

>\$125 Million invested to date

- Biotech: >\$90 Million
- Institutions: ~\$35 Million
- >70 financings of companies and assets
- >20 assets currently in active development

3 FDA-Approved Therapies

- Vyxeos (AML)
- Yescarta (DLBCL, tFL, PMBCL)
- Elzonris (BPDCN)

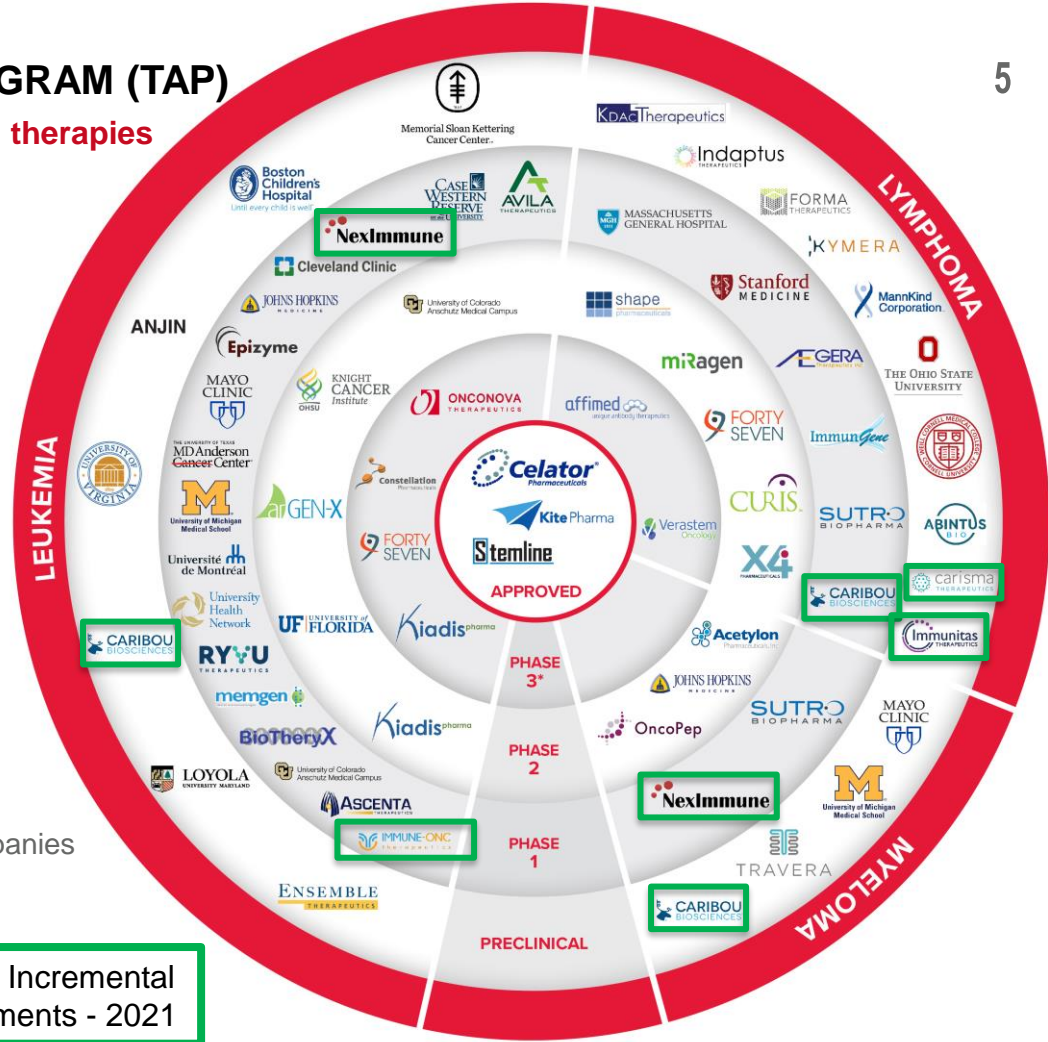
ROI Focus:

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

www.LLS.org/therapy-acceleration-program

BEATING CANCER IS IN OUR BLOOD.

New + Incremental Investments - 2021

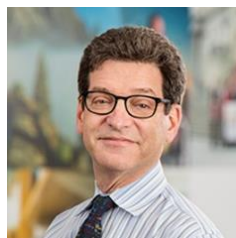


*Includes Phase 2 registration-enabling studies



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



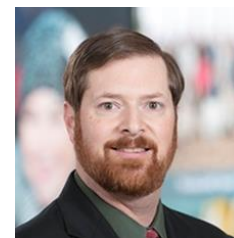
Lee Greenberger, PhD
SVP, Chief Scientific Officer

- 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

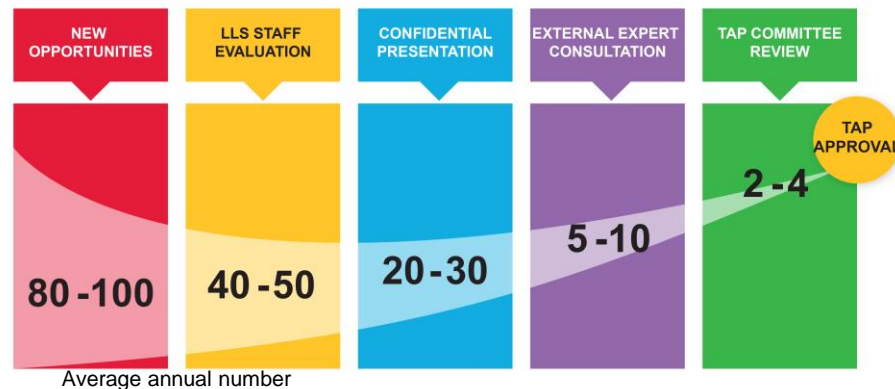
Therapy Acceleration Program Committee: <https://www.lls.org/therapy-acceleration-program/oversight>

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

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

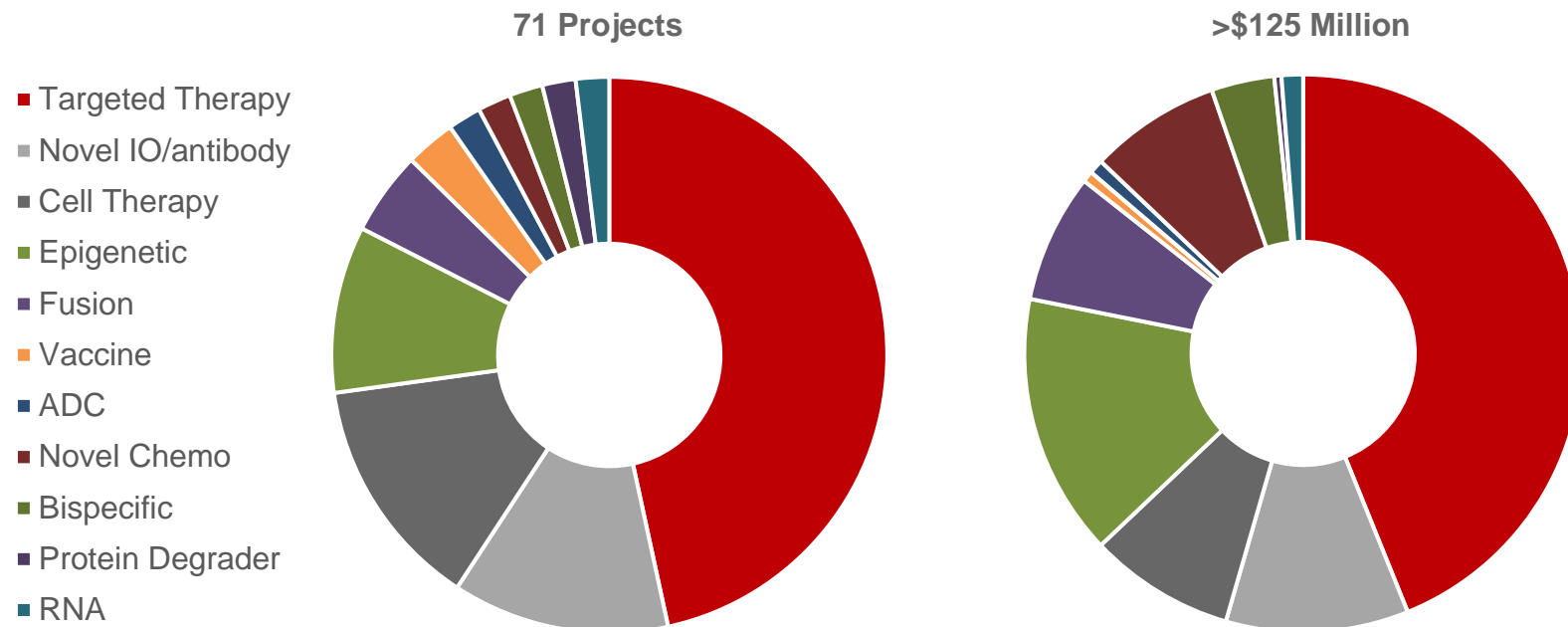
TAP-funded companies benefit from LLS blood cancer insight

- 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 (2007-2021)

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	FDA status
Magrolimab + Azacitidine	CD47 antibody	MDS				FortySeven ¹	
AFM13	CD30/CD16A bispecific engager	PTCL				affimed	
Pelabresib + Ruxolitinib	BET small molecule	MPN				Constellation ²	
Duvelisib	PI3Kδ/γ small molecule	PTCL				Verastem ³ Oncology	
Magrolimab + Rituximab	CD47 antibody	DLBCL			FortySeven ¹		
Cusatuzumab + Azacitidine	CD70 antibody	AML			argenx		
KO-539	Menin small molecule	AML		KURA ⁴ ONCOLOGY			
STRO-001	CD74 antibody drug conjugate	NHL/MM		SUTRO BIOPHARMA			(MM)
Mavorixafor + Ibrutinib	CXCR4 small molecule	Waldenström macroglobulinemia		X4 PHARMACEUTICALS			
RVU120	CDK8/19 small molecule	AML/MDS		RYVU 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		BioTherX			
BTX-A51	CK1-α/CDK7/CDK9 small molecule	AML/MDS		IMMUNE-ONC THERAPEUTICS			
IO-202	LILRB4 antibody	AML/CMML		CARIBOU BIOSCIENCES			
CB-010	CD19/PD1 KO allogeneic CAR	NHL					
KT-413	IRAK1MiD degrader	DLBCL	KYMERA				
KT-333	STAT3 degrader	Heme malignancies	Immunitas THERAPEUTICS				
IMT-009	CD161 antibody	NHL	ABINTUS				
TBD	<i>in vivo</i> CAR	TBD	carisma THERAPEUTICS				
TBD	CAR macrophage	TBD					

Orphan Drug Designation

Fast Track Designation

Breakthrough Therapy Designation

1: Acquired by Gilead ♦ 2: Acquired by Morphosys ♦ 3: Duvelisib acquired by Secura Bio ♦ 4: Licensed from University of Michigan

Updated August 2021

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 ¹ Kura ² Kymera ²
\$250-\$500 Million	Caribou ² Curis Forty Seven ³ Sutro
\$100-\$250 Million	Affimed BioTheryx ² Neximmune ² X4 ²
\$50-\$100 Million	Carisma ² Immune-Onc ² Immunitas ² Ryvu WindMIL ²
<\$50 Million	Abintus ² Indaptus ² OncoPep ²

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:

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Javeed Froozan, MBA 914.821.8817 | Javeed.Froozan@LLS.org





TAP SUCCESS STORIES

BEATING CANCER IS IN OUR BLOOD.



TAP SUCCESS: NOVEL LIPOSOMAL CYTOTOXIC THERAPY

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

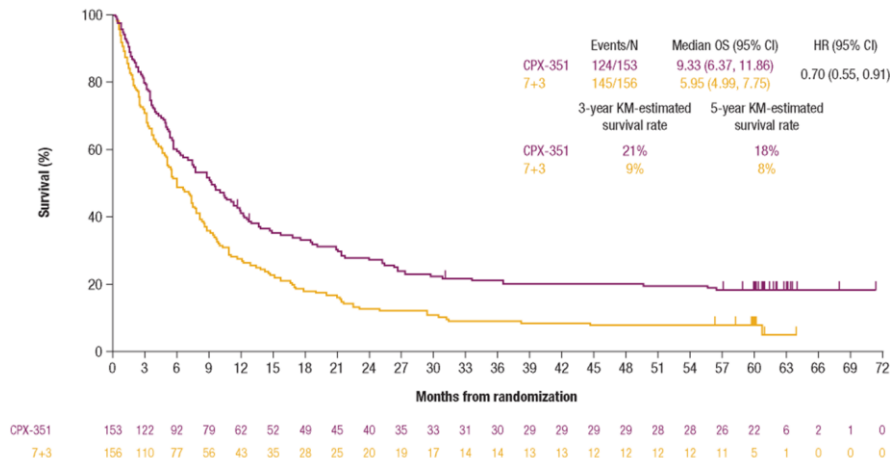


**ACQUIRED BY JAZZ PHARMA
FOR \$1.5 BILLION IN 2016**

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

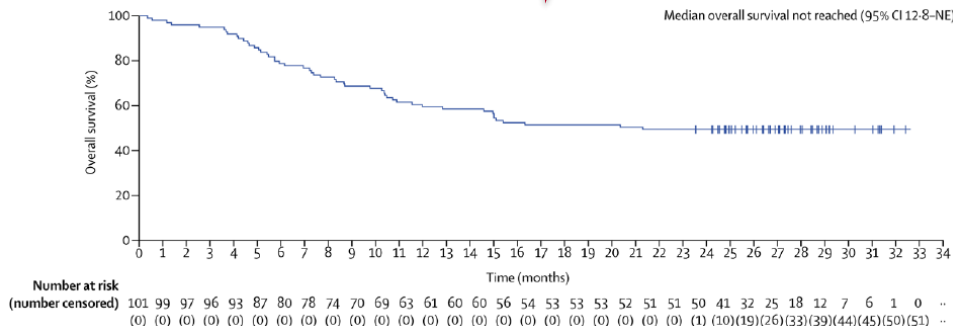
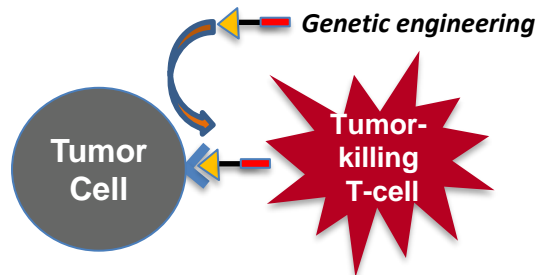


**ACQUIRED BY GILEAD
FOR \$11.9 BILLION IN 2017**

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)



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

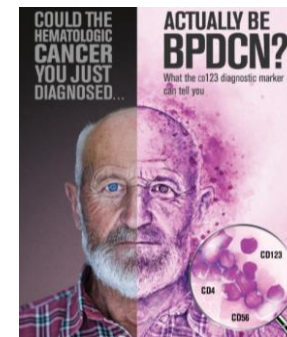
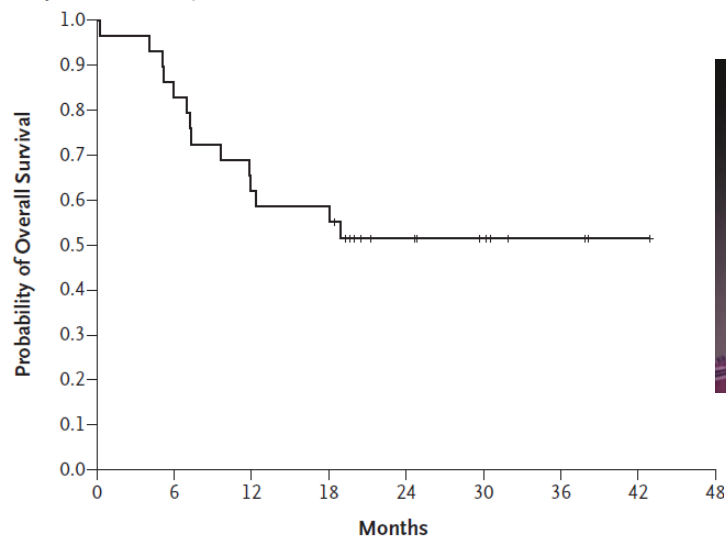
LLS TAP PROVIDED:

\$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

TAP SUCCESS: MAGROLIMAB (ANTI-CD47 ANTIBODY)

Magrolimab + Azacitidine induces high response rates in MDS and AML

Initiation of registration-enabling studies in 2020

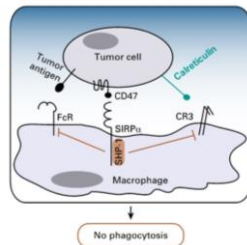


ACQUIRED BY GILEAD FOR \$4.9 BILLION IN 2020

LLS TAP PROVIDED:

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

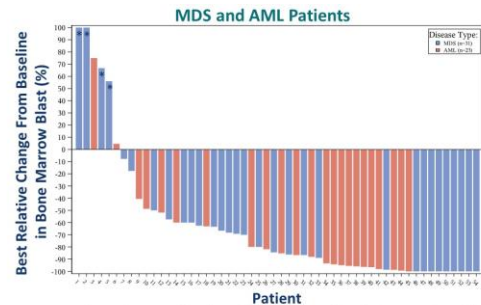
ROI: >\$40 MILLION



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%^{1,2})

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

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

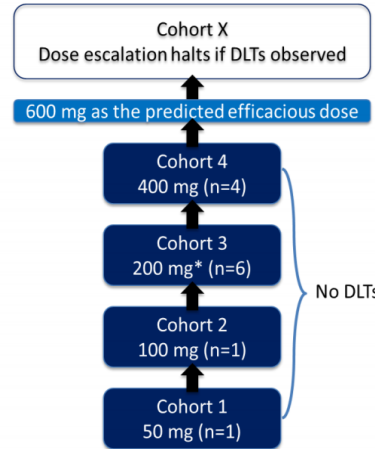
LLS TAP PROVIDED:

\$6.31 MILLION ASSET FUNDING TO U MICHIGAN

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

BEATING CANCER IS IN OUR BLOOD.

KO-539 Demonstrates Encouraging Early Clinical Activity



Clinical activities observed in 6 patients (efficacy evaluable = 8)				
Dose	Mutational Profile	CYP3A4 inhibitor	# of prior regimens	Clinical Activity
400 mg	RUNX1, SRSF2, ASXL1, TET2, STAG2, BCOR, PTPN11	Yes	3	Decreased peripheral blasts
200 mg	U2AF1, TET2, p53, DNMT3A, PTPN11	No	4	Stable disease
	NPM1, FLT3-ITD, TET2, CUX1	Yes	4	Morphological leukemia-free state
100 mg	NPM1, DNMT3A, KMT2D	Yes	7	CR, MRD-
100 mg	SETD2, RUNX1	Yes	2	CR, MRD+
50 mg	KMT2A-r	Yes	2	Decreasing hydra requirement

*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



ACQUIRED BY MORPHOSYS FOR \$1.7 BILLION IN 2021

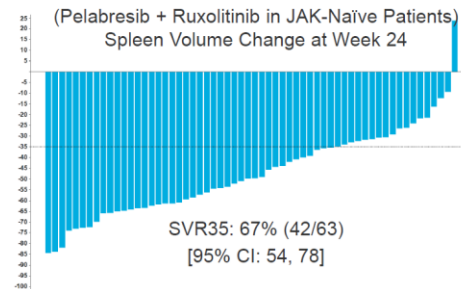
LLS TAP PROVIDED:

\$7.35 MILLION ASSET FUNDING

ROI: \$7.35 MILLION TO DATE

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

- 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)	COMFORT-1*	COMFORT-2**	SIMPLIFY-1***
24-Week SVR35 Rate	Upfront combo with ruxolitinib 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
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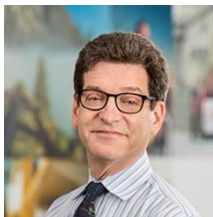
Robert Spiegel, MD
Spiegel Consulting LLC

David Weinstock, MD
Dana-Farber Cancer Institute

+ National Board Member

THANK YOU!

LLS Research Grants and TAP



Lee Greenberger, PhD
CSO & SVP Research



Michael Yaffe, PhD
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Erik Nelson, PhD
Exec. Dir. Research



James Kasper, MS
Exec. Dir. Research



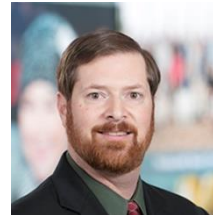
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Jun Xu, PhD
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