Lumosa Therapeutics (TPEX:6535)

Institutional Investor Conference

2024/11/29

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LT3001

Novel Small Molecule Entity for the Treatment of Acute Ischemic Stroke

Development progress: Phase 2 completed

Ischemic Stroke – Facts:
High Incidence Rate and Substantial Burden

Global

>7 million

new ischemic strokes each year

1 in 4 people

At risk of having a stroke in lifetime, the risk has increased by 50% in the last 17 yr

#1

cause of long-term severe disability

~US$14 billion

total cost of stroke globally in 2017

Global Stroke Fact Sheet 2022

USA

>500 thousand

new ischemic strokes each year

Every 40 seconds

someone in the US has a stroke

$56 billion

Cost of stroke for US residents between 2019~2020

<20%

of AIS patients receive thrombolytic agents to recanalize occluded blood vessels

CDC. Gov

1.World stroke organization fact sheet 2022
2.Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association, PMID: 36695182
3.https://www.cdc.gov/stroke/facts.htm

Acute Ischemic Stroke – Limitations of Current Treatment Options Underscore Urgent Need for Better Alternatives

	Large vessel occlusion	Small vessel occlusion	Lacunar infarction
<4.5 hr	IV rtPA		
4.5 ~ 24 hr	IA EVT	LT3001 alone (1) Novel Reperfusion Therapy for Patients Ineligible for IV tPA and EVT 205, Phase 2 (US, EU, TW) 202, Phase 2 (CN)	
	+LT3001 (2) Enhance EVT outcomes 203, Phase 2 (US, TW)		

Limitations of Current Standard of Care

IV tPA

- <20% AIS patient can be treated
- 10x increased sICH incidence rate (6.4% vs 0.6% placebo, $p<0.001$)
- ~30% patients can be treated (30% vs 20% placebo, $p<0.05$)

IA EVT

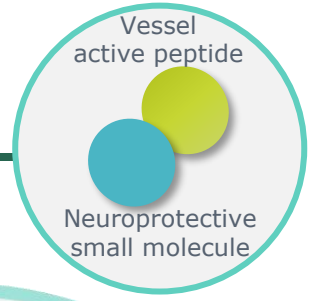
- <10% AIS patients can be treated
- <50% patients can be treated (46% vs 29% placebo)

LT3001 Objective

1. Extend treatment window beyond 4.5 hr post-stroke threshold
2. Synergistic application with EVT to optimize current treatment efficacy

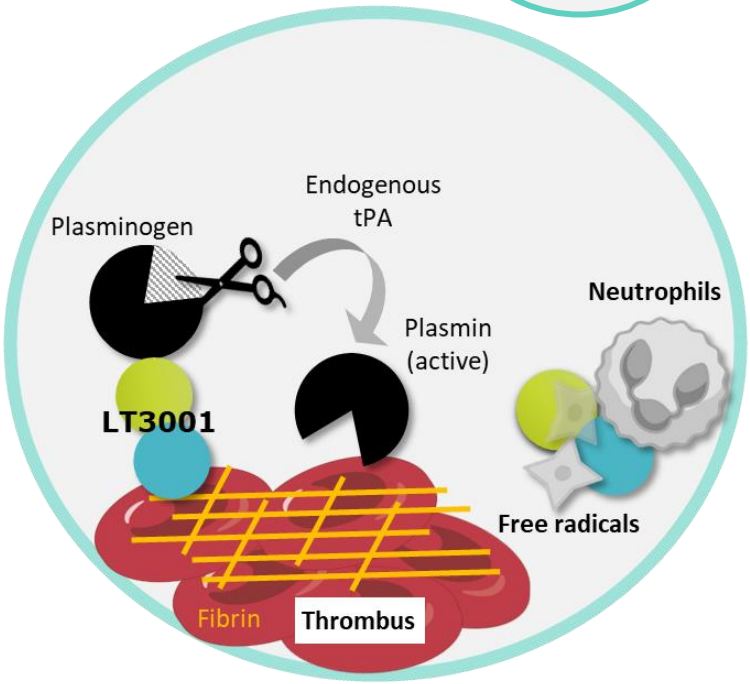
1. NINDS, N Engl J Med 1995; 333:1581-1588
2. HERMES meta-analysis. Lancet 2016; 387: 1723–31
3. Nationwide private health insurance database, 2012-2018, US. Neurosurg Focus. 2021 Jul;51(1):E2

LT3001 With Unique Dual-Action Mechanism Differentiates from Competitors



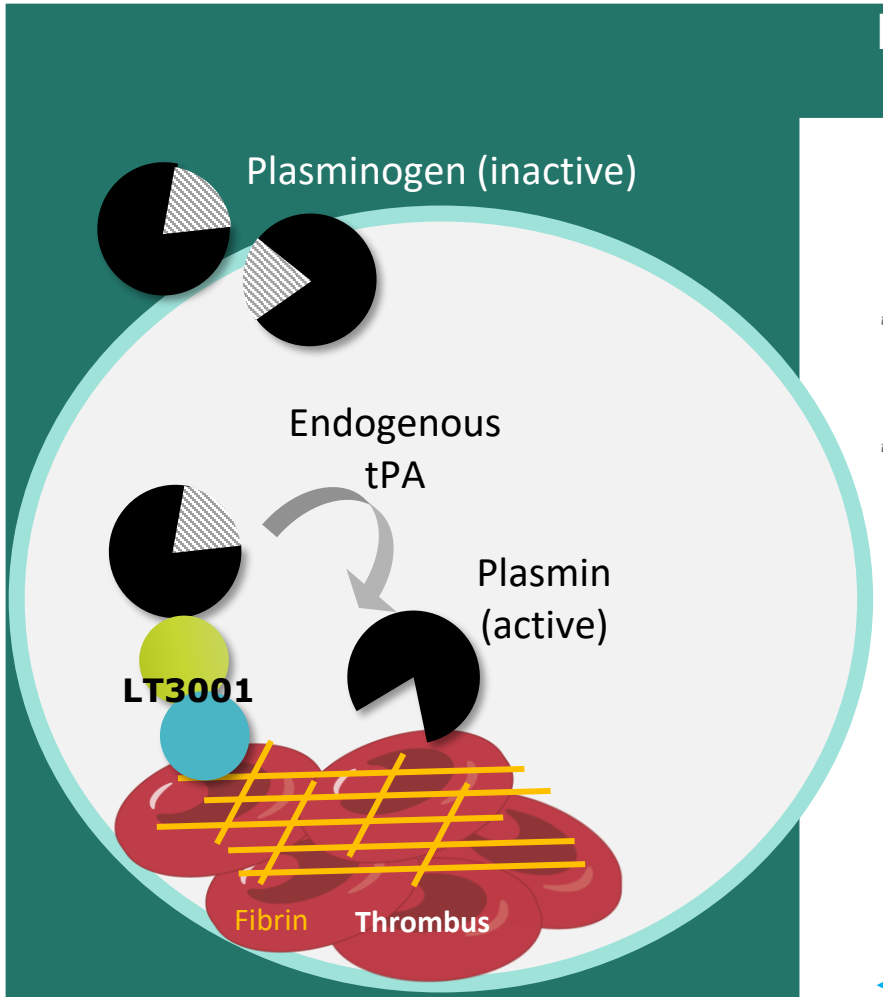
LT3001 Advantages

1. **Innovative Mechanism and Administration Design:** Using endogenous tPA to achieve thrombolysis without compromising coagulation function while simultaneously eliminating neurotoxic free radicals and reducing inflammatory response. Providing more comprehensive treatment during the critical three-day window post-stroke with its dual-action thrombolytic and neuroprotective functions.
2. **Breakthrough Phase 2a Results:** Received FDA Fast Track designation and successfully licensed to Shanghai Pharma in China.
3. **Comprehensive Phase II Clinical Trial Strategy:** Concurrent development in US, China, Europe, and Taiwan, focusing on moderate to severe stroke patients, with the use of advanced imaging technology for patient selection and outcome assessment



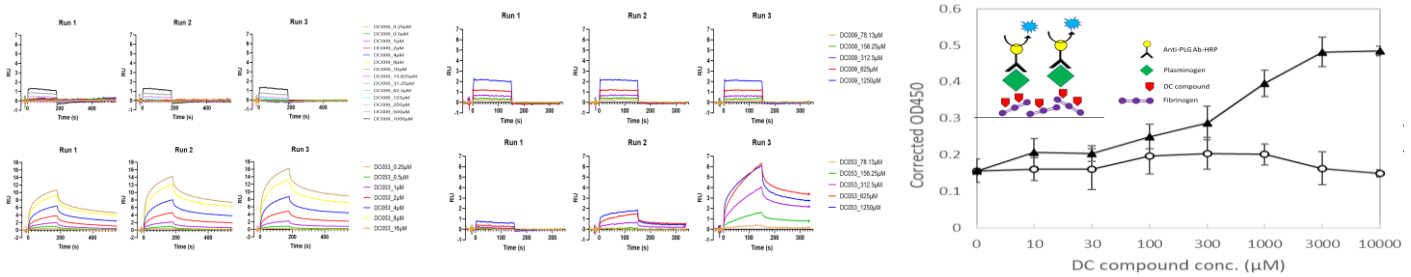
Product	Thrombolysis	Cell Protection	Dosing regimen	Tx time window	Development stage	Company
Alteplase (rt-PA)	✓	✗	Single	< 4.5hr	Marketed	Roche/ Genentech
LT3001	✓	✓	Multiple	< 24hr	Phase 2 (US, EU, CN, TW)	Lumosa Therapeutics
TMS-007	✓	✓	Single	< 12hr	Phase 2 completed (JP)	Biogen → Corxel
DM-199	✗	✓	Single	< 24hr	P2/3 (US)	DiaMedica
Edaravone	✗	✓	Multiple	< 24hr	Marketed (CN, JP)	Mitsubishi Tanabe

LT3001 MOA: Enhance Endogenous Thrombolytic Response

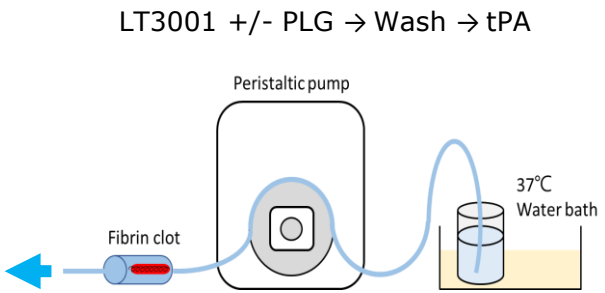


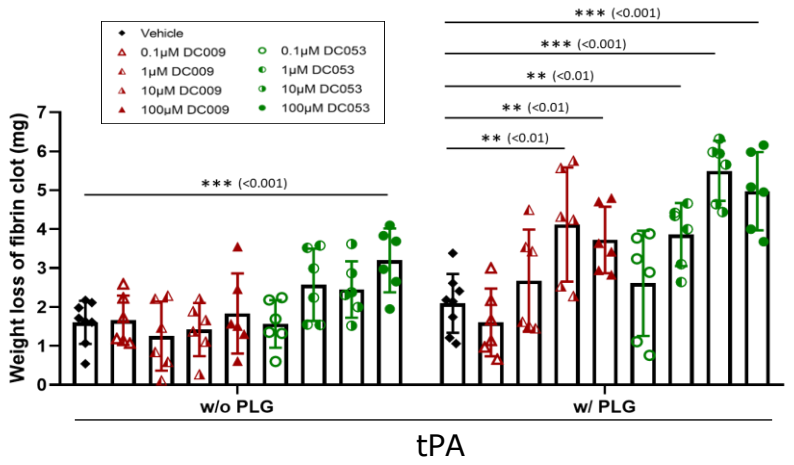
LT3001 Promotes Fibrinolytic Protein-Thrombus Binding to Amplify Thrombolytic Efficacy

Promote plasminogen-fibrinogen binding



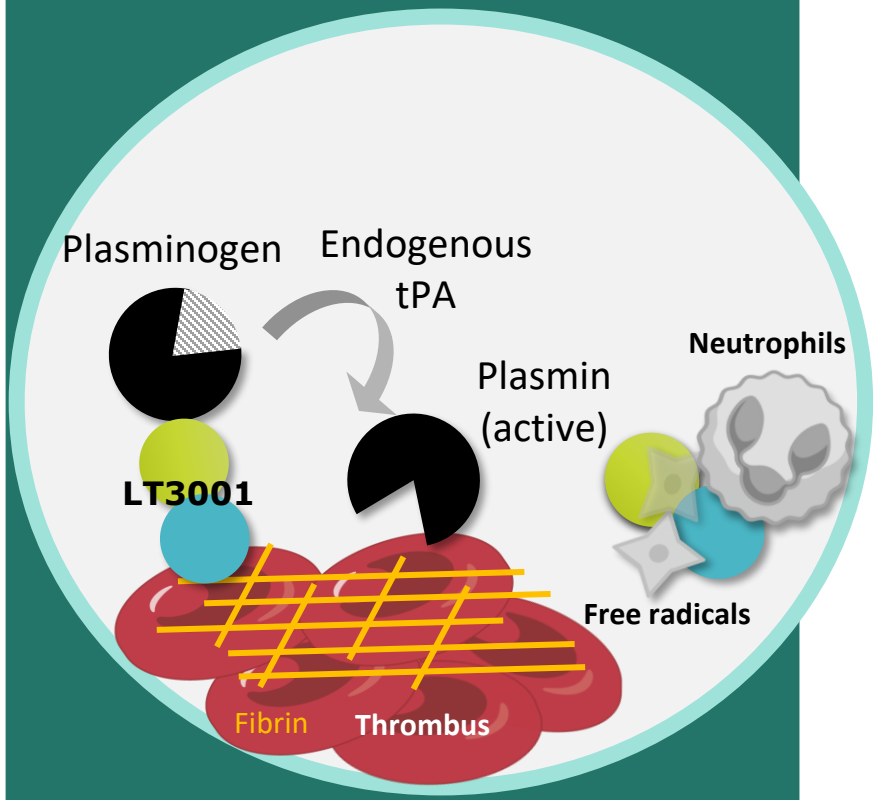
LT3001 Enhances endogenous thrombolytic response



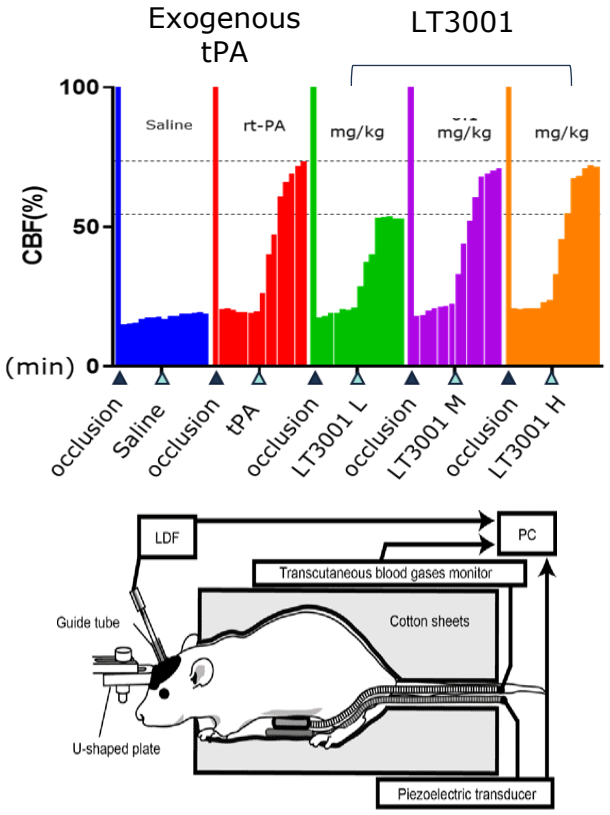


LT3001 MOA: Breakthrough Thrombolysis Mechanism – Restoring Blocked Blood Flow w/o Hemorrhagic Complications

Leveraging Native Thrombolytic Pathways to Dissolve Blood Clots and Restore Blood Flow without Hemorrhagic Complications

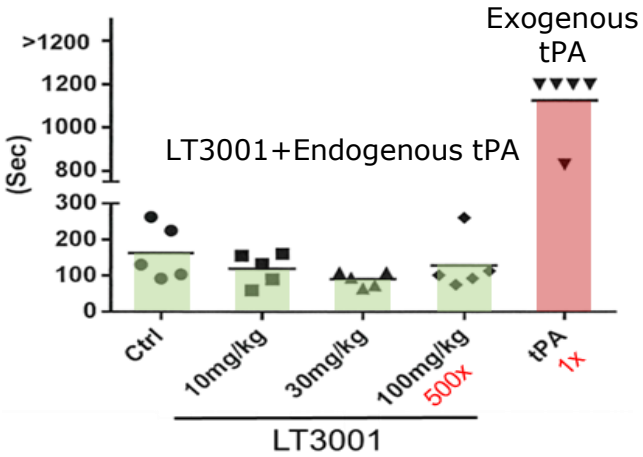


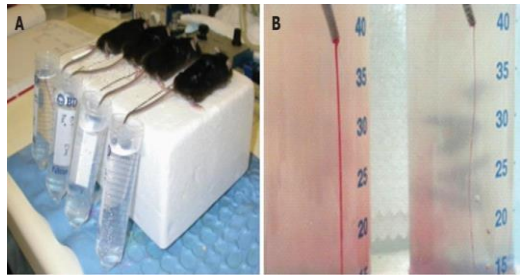
Restore occluded cerebral blood flow



Front. Biosci. (Elite Ed) **2014**, 6(1), 62–68

Preserves the integrity of coagulation function

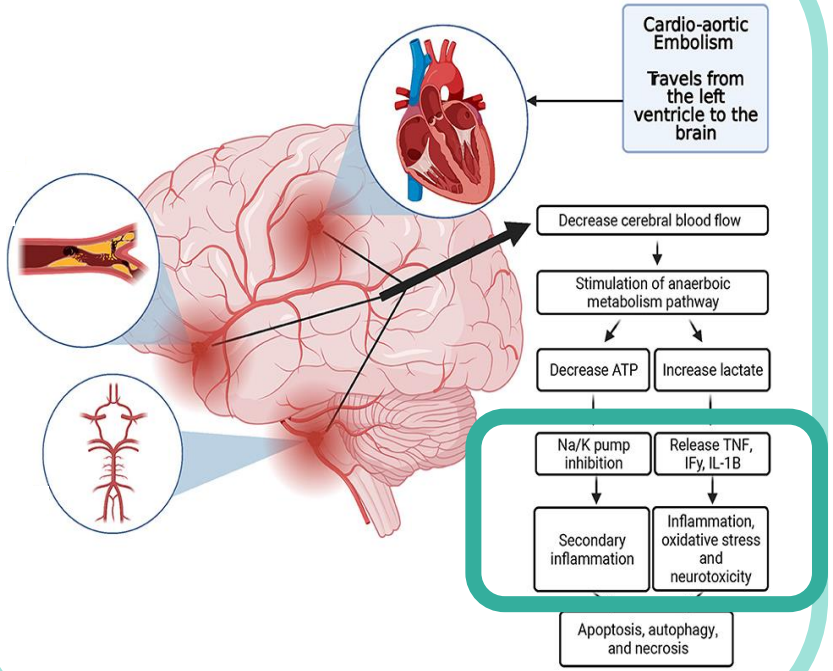




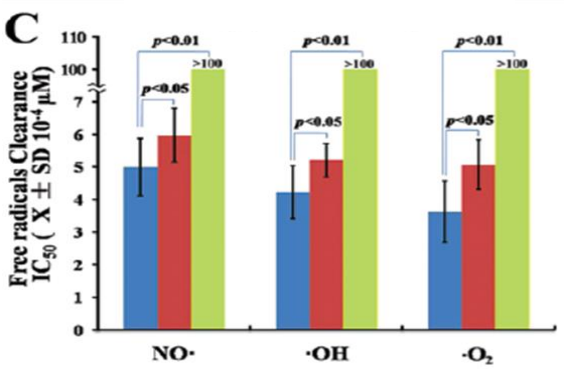
Liu Y. et al.,*World J Exp Med* 2012; 2(2): 30-36

LT3001 MOA: Protecting Cells, Minimizing Secondary Damage During Blood Flow Restoration

Neutralizing Free Radicals Post-Stroke and Mitigating Inflammatory Cascades

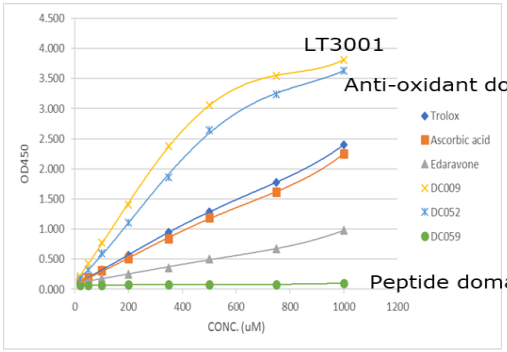


Comprehensive Free Radical Elimination



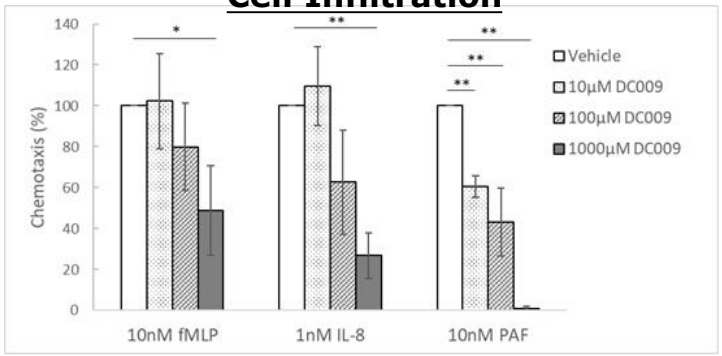
J. Mater. Chem. B, 2016, 4, 5991--6003

Suppress Oxidative Stress Reactions



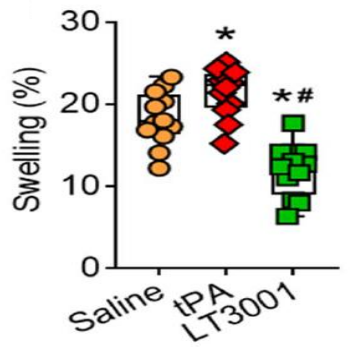
Report: LR-19-0011

Inhibit Inflammatory Cell Infiltration



Report: LR-21-0008

Mitigate Post-Stroke Cerebral Edema



Transl. Stroke Res. (2022)

Front. Neurol., 31 May 2022 Sec. Stroke Volume 13 - 2022 | https://doi.org/10.3389/fneur.2022.870141

Comprehensive Trial Strategy, Positive Phase 2a Outcome

Pivotal Phase 2 Trial in China to be Unblinded by the end of 2024, Phase 3 Trial to be Initiated 2025~2026

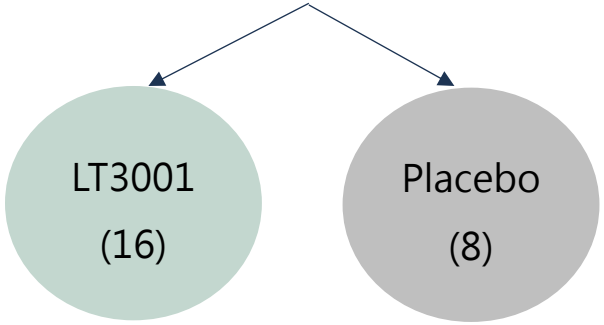
Phase 1: US, TW

Study no.	Dosing Regimen		
LT3001-101 (US, n=16)	Single dose	1x	15-Min. IV infusion
		2x	15-Min. IV infusion
LT3001-105 DDI (US, n=65)	3-Day multi-dose	1x	15-Min. IV infusion
LT3001-103 (CN, n=24)	3-Day multi-dose	1x	15-Min. IV infusion
		2x	30-Min. IV infusion

1. PK profile suitable for acute phase drug development
   - Rapid clearance, no accumulation, linear absorption-dose relationship
2. Flexible dosing strategy
   - May be administered for 3 consecutive days
   - Compatible with commonly prescribed antiplatelet and anticoagulation medications
3. No racial/ethnic differences

Phase 2a: US, TW

24 AIS Patients



Single-dose of LT3001 administered to AIS patients beyond the standard tPA treatment window (within 24 hrs)

1. Favorable safety profile demonstrated
   - No observable increase in sICH
2. Trend in therapeutic efficacy
   - Enhanced neurological function improvement
   - Higher proportion of patients achieved return to normal daily activities post-treatment (mRS(0-1): 21% vs 14%)

Phase 2: US, EU, CN, TW

202, Phase 2, multi-dose (CN, n=300)
Tx window: <24 hr
Illegible for tPA/EVT
Low dose : high dose : placebo=1:1:1

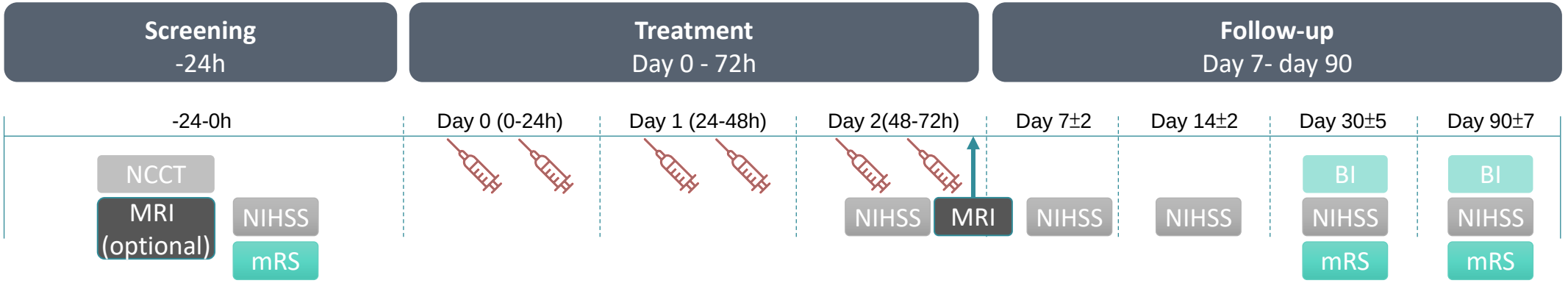
205, Phase 2, multi-dose (US, EU, TW, n=200)
Tx window: <24 hr
Illegible for tPA/EVT
Imaging-based screening criteria

203, Phase 2 (US, TW, n=24)
Tx window: <24 hr
Illegible for tPA/EVT
Concurrent use of mechanical thrombectomy

LT3001-202 Phase II Study Results

Shanghai Pharma has completed a multi-center, randomized, double-blind, placebo-controlled Phase II clinical trial

LT3001-202: Design – A Multi-center, Randomized, Double-blind, Placebo-controlled Phase II Study



Primary inclusion/ exclusion criteria

- Age: 18-80
- AIS patients
- NIHSS score 4-25 at time of randomization
- Able to receive study drug within 24 hrs of onset
- Exclude patients who have received or plan to receive EVT or IV tPA

Randomization

N=300
1:1:1

- LT3001, 0.025 mg/kg
- LT3001, 0.050 mg/kg
- Placebo

30min-IV infusion

Central randomized with stratification factor of ① baseline MRI (Y/N), ②baseline NIHSS of 4~6, 7~10, 11~25

- **Primary endpoint – Safety**
  - Safety: treatment emergent adverse events (TEAE) and treatment-related adverse events (TRAE) within 90 days of dosing, incidence and rates of symptomatic or asymptomatic intracranial hemorrhage within 3 days
- **Secondary endpoint – Efficacy**
  - Functional outcome (mRS)
  - Neurobehavioral improvements (NIHSS)
  - Activities of daily living (BI)

Completed 300 enrollments in 34 centers during 2023/4-2024/7

LT3001-201 (P2a Single-dose) vs LT3001-202 (P2b Multi-dose)

Category	Comparative parameters	LT3001-201 (P2a, US/TW)		LT3001-202 (P2b, CN)	
		LT3001 Alone	Placebo	LT3001 Multi-dose	Placebo
Subject characteristics	Cases	16	8	200	100
	Age (yr, median)	62	69	64	
	Gender distribution (Male %)	75%	88%	70%	
	Time from onset to first dose (hr, median)	19.4	18.0	12.1	
	Baseline NIHSS score (median)	6	4	8	8

LT3001-202: Study Results

- **Primary Endpoint Assessment:**
  - LT3001 demonstrates robust overall safety and tolerability.
  - Adverse event and adverse reaction rates within 90 days of first dosing were comparable across high-dose LT3001, low-dose LT3001, and placebo groups, with the majority being mild to moderate in severity.
  - No symptomatic intracranial hemorrhages observed across all groups; only 3 asymptomatic intracranial hemorrhages reported, all in the placebo group.
- **Key Secondary Endpoints** :
  - LT3001 showed preliminary efficacy, with subjects showing promising proportion of functional recovery (mRS 0-1) at Day 90 post-treatment, indicating return to normal daily living capabilities.

AIS Clinical Trial Data Comparison –
Pivotal Studies on Thrombolytic Agents

MOA	Trial	Tx Window	Adv. img. screen	Sample size	Baseline stroke severity[4]	% mRS=0-1 on day 90 (efficacy)					sICH (risk of bleeding)			
Traditional thrombolytics (tPA, TNK)	**PRISMS, 2018** (mild stroke)	0-3 hr	None	156/157	2/2[5]	**IV tPA**	**Aspirin**		**Δ**	**P value**	**IV tPA**	**Aspirin**		**Δ**
						78%	82%	**-4%**	Avg. fxn recovery improv. 6%	NA	3.2%	0%	**3%**	Avg. sICH increase 3%
	NINDS, 1995 (marketed)	0-3 hr	None	168/165	14/14	**IV tPA**	**Placebo**				**IV tPA**	**Placebo**		
						39%	26%	**13%**		0.02	6.4%	0.6%	**6%**	
	ECASS III, 2007 (Extends guideline tx window to 4.5h)	3-4.5 hr	None	418/403	9/10	**IV tPA**	**Placebo**				**IV tPA**	**Placebo**		
						52%	45%	**7%**		0.04	2.4%	0.2%	**2%**	
	EPITHET, 2008 (Neuroimaging reveals salvageable tissue potential: 90%/none:10%)	3-6 hr	Yes/none	52/49	5/5		**tPA**	**Placebo**				**IV tPA**	**Placebo**	
							44%	42%	**2%**					
						Screened	45%[3]	40%[3]	5%		7.7%	0%	**8%**	
						Not screened	38%[3]	60%[3]	-22%					
	Extend, 2019 (Neuroimaging reveals salvageable tissue potential)	3-9 hr	Yes	113/112	12/10	**IV tPA**	**Placebo**				**IV tPA**	**Placebo**		
						35%	30%	**6%**		0.04	6.2%	0.9%	**5%**	
	Wake-Up, 2019 (Neuroimaging reveals salvageable tissue potential)	Median 10 hr	Yes	254/249	6/6	**IV tPA**	**Placebo**				**IV tPA**	**Placebo**		
						53%	42%	**11%**		0.02	2.4%	0.4%	**2%**	
	TRACE 3, 2024 (Neuroimaging reveals salvageable tissue potential)	0-24 hr	Yes	264/252	11/10	**IV TNK**	**Placebo**				**IV TNK**	**Placebo**		
						33%	24%	**9%**		0.03	3%	0.8%	**2%**	

[1]cerebral hemorrhage; [2]Edaravone-Dexborneol;[3]mRS=0-2 ;[4]NIHSS baseline, median value; [5]mean value

AIS Clinical Trial Data Comparison –
Pivotal Studies on Thrombolytic Agents vs LT3001

MOA	Trial	Tx Window	Adv. img. screen	Sample size	Baseline stroke severity[4]	% mRS=0-1 on day 90 (efficacy)					sICH (risk of bleeding)			
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						33%	24%	**9%**		0.03	3%	0.8%	**2%**	
Innovative thrombolysis w/ cell protection LT3001	**LT3001-202, 2024** (Ph2, no tPA/EVT)	**0-24 hr**	**No screening**	100/group	8/8	**LT3001**	**Placebo**				**LT3001**	**Placebo**		
						LT3001 demonstrates promising efficacy trend					No increased risk of ICH			0%

[1]cerebral hemorrhage; [2]Edaravone-Dexborneol;[3]mRS=0-2 ;[4]NIHSS baseline, median value; [5]mean value

LT3001-202 Phase 2 Clinical Trial Outcomes

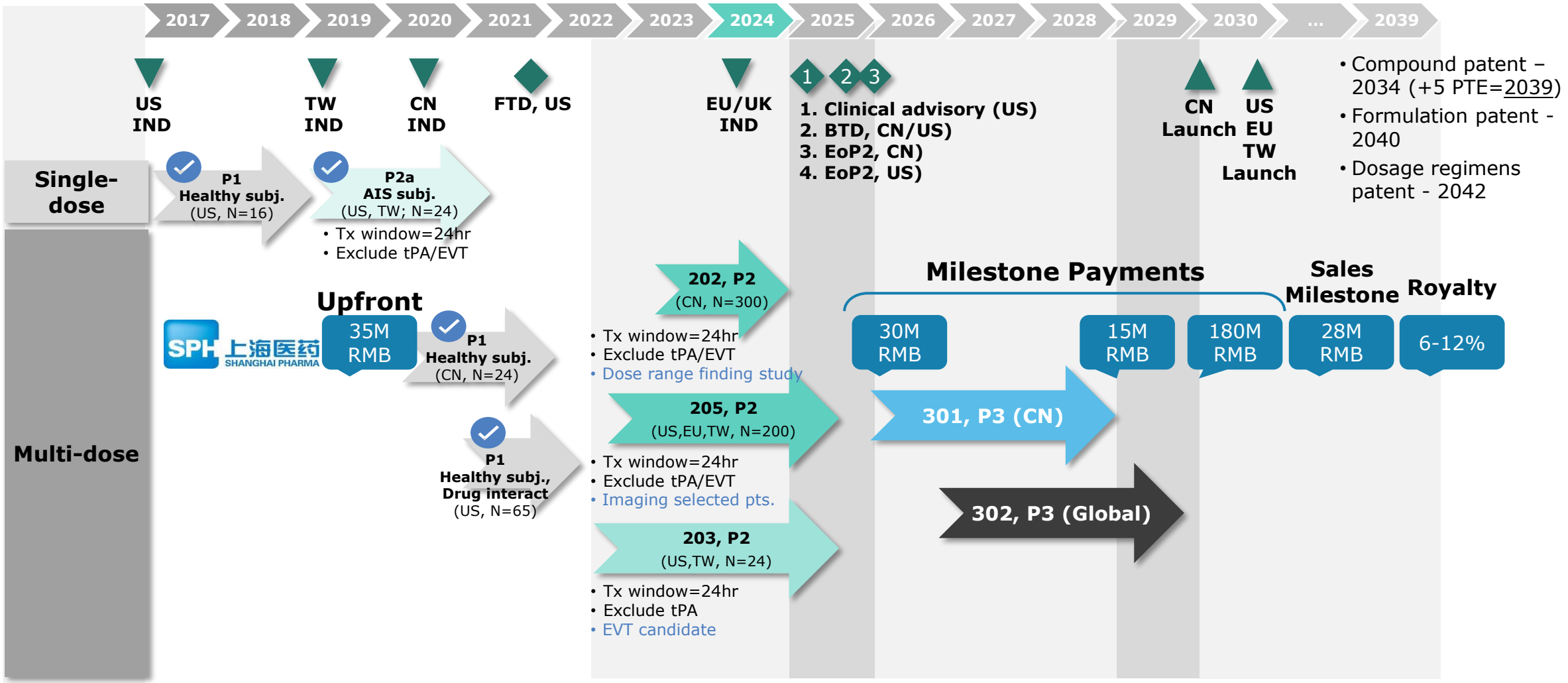
Advancing development milestones

- Progressed from 24-patient Phase 2a exploratory trial to successful concept validation in 300-patient Phase 2b study.
- Safety and efficacy validated through partner-led clinical trials.
- Confirmed LT3001’s mechanism in AIS patients, demonstrating superior efficacy and safety compared to traditional thrombolytic agents in target patient population.

Validating product value

- Treatment window extended to 24 hrs – 5x longer than tPA’s 4.5-hr window.
- Efficacy and safety demonstrated in patients without advanced imaging screening, enhancing clinical application potential.

LT3001 Clinical Trial Plan –
Anticipated P3 Initiation 2025-2026



LT3001 Novel Entity:
Addressing a 30-year Unmet Medical Need

Key Advantages

- **Innovative Dual MOA –** Novel thrombolytic with low bleeding risk + neuroprotective effects
- **Addressing Unmet Medical Needs –**
  - Significantly extended acute stroke treatment window from 4.5 to 24 hours
  - Trial design includes monotherapy and combination with mechanical thrombectomy, potentially applicable to over 80% of AIS patients
  - Flexible dosing strategy, compatible with common antiplatelet and anticoagulation medications
- **Clinical concept validation complete**

Strong Market Potential

- **Potential Market Size -** Over 7 million acute ischemic stroke patients globally per year; more than 80% currently untreated with thrombolytics, representing significant market opportunity
- **Comprehensive Patent Protection -** Compound patent protection through 2039, formulation and method-of-use patents through 2042
- **High Market Expectations -** US/EU market research indicates high physician prescription intent; payer estimated price per treatment approximately USD 25,000.

Steering Committee

LT3001-202
Principal Investigator

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Thank You