# LOTIS

# Loncastuximab Tesirine Clinical Assessments

For information about the LOTIS Clinical Trial Program, email ADC Therapeutics at medicalinformation@ADCTherapeutics.com

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Innovating Science. Inspiring Hope.

# Loncastuximab tesirine (Lonca; loncastuximab tesirine-lypl) indication

Loncastuximab tesirine-lpyl (Zynlonta, ADC Therapeutics SA) is a CD19-directed antibody and alkylating agent conjugate indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after ≥2 lines of systemic therapy, including DLBCL not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

This indication is FDA-approved under accelerated approval based on ORR. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

# The LOTIS Clinical Development Program

## LOTIS-1
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1, open-label, dose-escalation, dose-expansion study to evaluate the tolerability, safety, PK, and efficacy of loncastuximab tesirine in patients with R/R B-NHL

**NCT02669017**

**COMPLETED**

## LOTIS-2
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, open-label, single-arm study to evaluate the efficacy and safety of loncastuximab tesirine in patients with R/R DLBCL

**NCT03589469**

**ACTIVE, NOT RECRUITING**

## LOTIS-3
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1/2, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and ibrutinib in patients with advanced DLBCL or MCL

**NCT03684694**

**RECRUITING**

## LOTIS-4
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and durvalumab in patients with advanced DLBCL, MCL, or FL

**NCT03685344**

**TERMINATED**

## LOTIS-5
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 3, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab versus immunochemotherapy in patients with R/R DLBCL

**NCT04384484**

**RECRUITING**

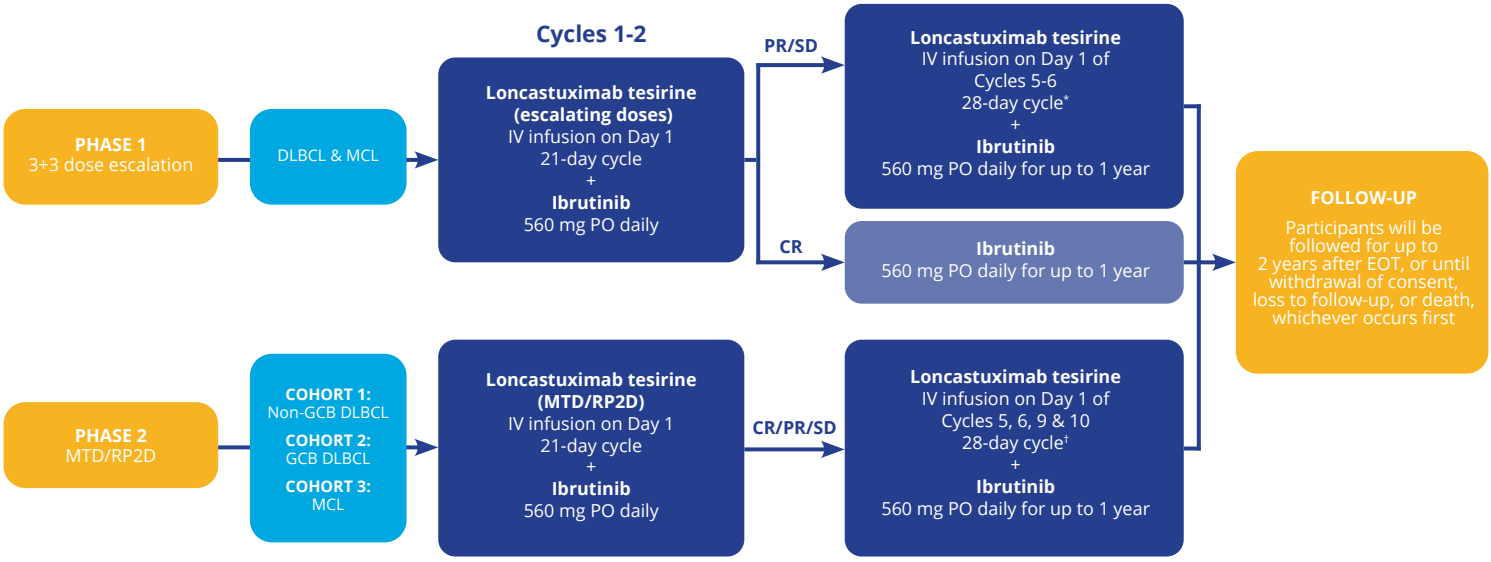
## LOTIS-6
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine versus idelalisib in patients with R/R FL

**NCT04699461**

**RECRUITING**

# A Phase 1/2, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and ibrutinib in patients with advanced DLBCL or MCL




## PRIMARY ENDPOINT

- Phase 1: AEs, AEs ≥Grade 3, SAEs, SAEs ≥Grade 3; DLTs, dose modifications
- Phase 2: CRR‡ determined by the IRC. CRR, defined as the number of participants with a BOR of CR in the non-GCB DLBCL cohort only

## KEY SECONDARY ENDPOINTS

- Phase 1: ORR‡, defined as the number of participants with a BOR of CR or PR; DOR; RFS; PFS; OS; PK
- Phase 2: ORR‡,defined as the number of participants with a BOR of CR or PR
- Phase 2: CRR in GCB DLBCL, all DLBCL, and MCL participants. CRR determined by the investigator and/or IRC. CRR‡, defined as the number of participants with a BOR of CR in non-GCB DLBCL, GCB DLBCL,all DLBCL, and MCL participants
- Phase 2: ORR; DOR; RFS; PFS; OS; PK; CRR in subgroups; HRQoL, safety (AEs, AEs ≥Grade 3, SAEs, SAEs ≥Grade 3)

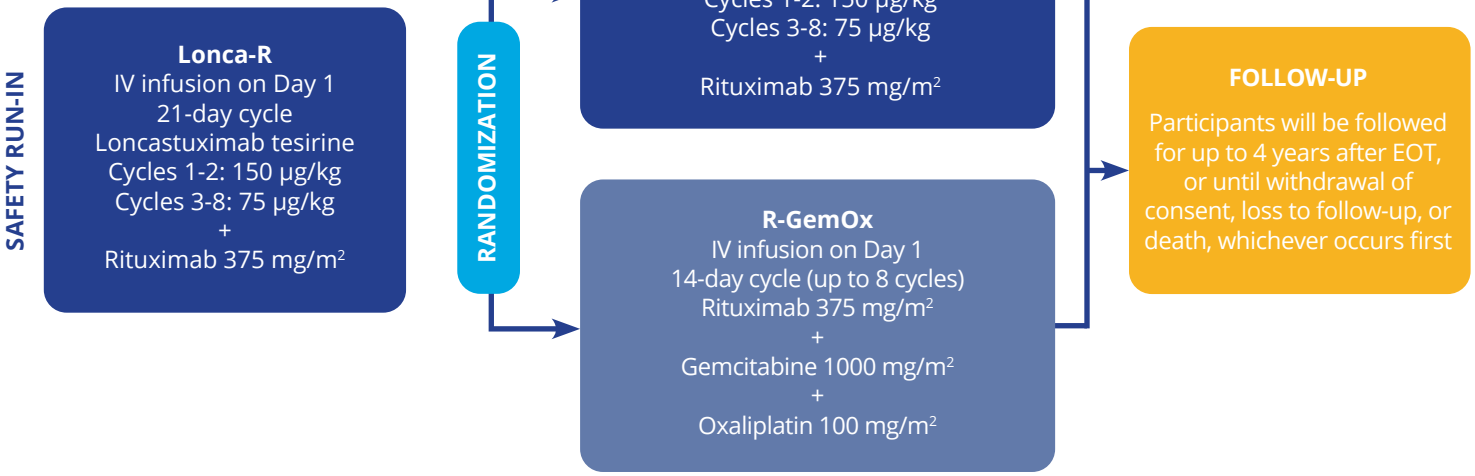
## KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- Pathologic diagnosis of DLBCL or MCL
- Participants with DLBCL must have relapsed or refractory disease and have failed, or been intolerant to, available standard therapy
- Participants with MCL must have relapsed or refractory disease and have received ≥1 prior line of therapy
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- AHCT or alloHCT permitted if received ≥60 days prior to the start of study drug
- No prior loncastuximab tesirine or BTK inhibitors
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*Break from loncastuximab tesirine treatment on cycles 3-4.
†Break from loncastuximab tesirine treatment on cycles 3-4 and 7-8.
‡According to the 2014 Lugano Classification.
Ibrutinib is supplied by Pharmacyclics LLC.

LOTIS-3
LOncastuximab Tesirine ClinIcal AsSessment

# A Phase 3, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab versus immunochemotherapy in patients with R/R DLBCL




## PRIMARY ENDPOINT

- PFS

## KEY SECONDARY ENDPOINTS

- OS
- ORR*
- CRR*
- DOR
- Number of participants who experience ≥1TEAE and/or SAE
- PK
- HRQoL

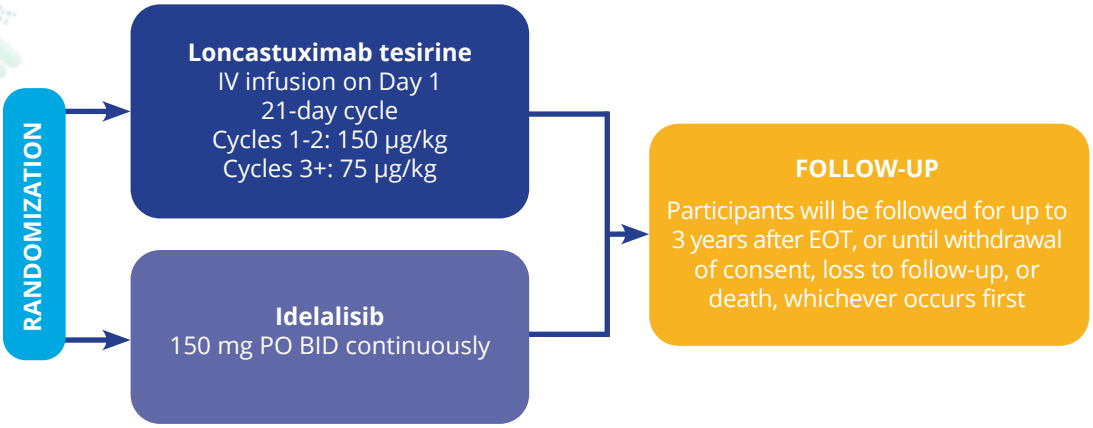
## KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, or high-grade B-cell lymphoma with *MYC* and *BCL-2* and/or *BCL-6* rearrangements
- Relapsed or refractory disease following ≥1 multi-agent systemic treatment regimens
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- AHCT or alloHCT permitted if received ≥30 days or ≥60 days prior to the start of study drug, respectively
- No prior loncastuximab tesirine or R-GemOx
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*According to the 2014 Lugano Classification.

LOTIS-5
LOncastuximab Tesirine ClinIcal AsSessment

# A Phase 2, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine versus idelalisib in patients with R/R FL




**PRIMARY ENDPOINT**
- CRR*

**KEY SECONDARY ENDPOINTS**
- ORR*
- PFS
- OS
- DOR
- Number of participants who experience ≥1 TEAE and/or SAE
- PK
- HRQoL

**KEY ELIGIBILITY CRITERIA**
- ECOG PS 0 to 2
- Pathologic diagnosis of FL (Grade 1, 2, 3a)
- Participants with FL which has transformed to DLBCL or other aggressive lymphomas are not eligible
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- Relapsed or refractory disease following ≥2 prior treatment regimens, including ≥1 anti-CD20 therapy
- AHCT or alloHCT permitted if received ≥30 or ≥60 days prior to start of study drug, respectively
- No prior loncastuximab tesirine or idelalisib
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*According to the 2014 Lugano Classification.

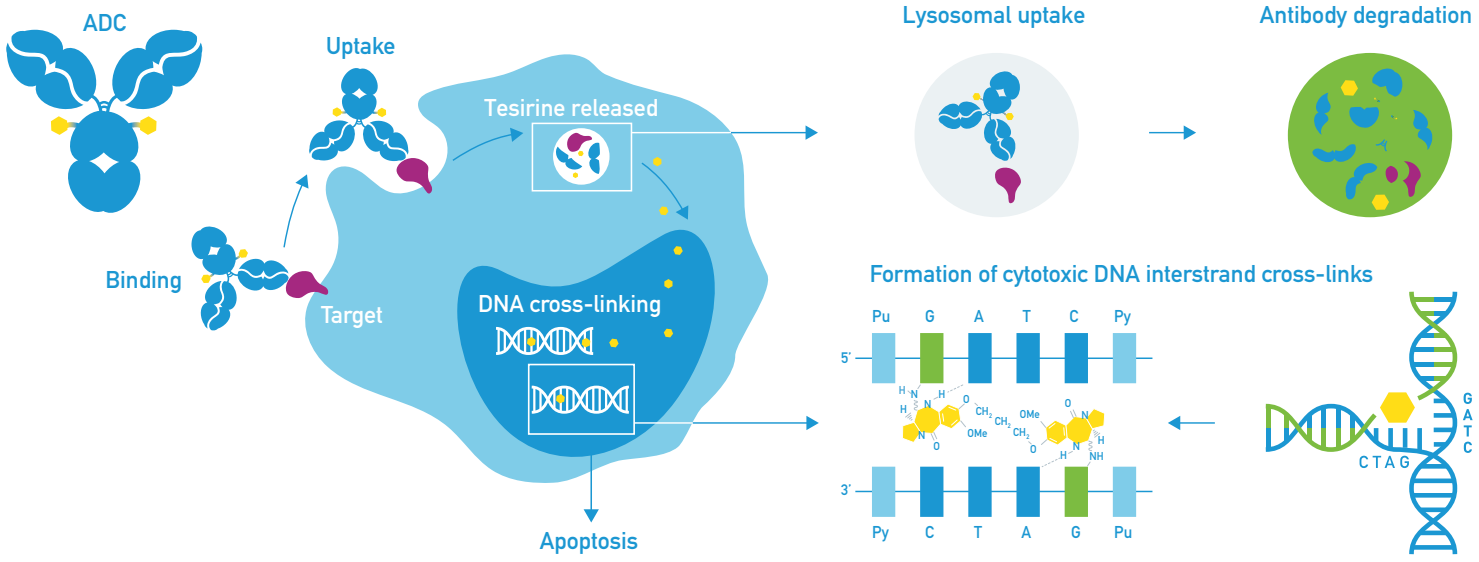
LOTIS-6
LOncastuximab Tesirine ClinIcal AsSessment

# ADC Therapeutics is advancing next-generation PBD-based ADCs

ADC Therapeutics is leading the development and commercialization of next-generation ADCs with highly potent and targeted PBD dimer technology. These PBD-based ADCs are expected to provide a novel way to treat hematological cancers and solid tumors, address significant unmet medical needs, and improve the lives of people with cancer.

## An MOA that features the "stealth-like" properties of PBD dimer toxins

- The antigen-targeted antibody binds to a specific tumor cell surface antigen and internalizes the drug conjugate
- The potent PBD dimer is released inside the cell, where it then creates a covalent cross-link between the strands of the DNA double helix
- Because the cross links formed by the PBD dimer are relatively non-distorting to the DNA structure, they are invisible to repair mechanisms and can covertly persist to interrupt cell division




LOTIS
LOncastuximab Tesirine ClinIcal AsSessment

# Abbreviations

ADC, antibody drug conjugate
AE, adverse event
AHCT, autologous hematopoietic cell transplantation
AlloHCT, allogeneic hematopoietic cell transplantation
BID, twice daily
B-NHL, B-cell non-Hodgkin lymphoma
BOR, best overall response
BTK, Bruton tyrosine kinase
CD, cluster of differentiation
CNS, central nervous system
CR, complete response
CRR, complete response rate
DLBCL, diffuse large B-cell lymphoma
DLT, dose-limiting toxicity
DOR, duration of response
ECOG, Eastern Cooperative Oncology Group
EOT, end of treatment
FDA, Food and Drug Administration
FL, follicular lymphoma
GCB, germinal center B-cell-like
HCT, hematopoietic cell transplantation
HRQoL, health-related quality of life
IRC, Independent Review Committee
IV, intravenous
Lonca, loncastuximab tesirine
Lonca-R, loncastuximab tesirine and rituximab
MCL, mantle cell lymphoma
MOA, mechanism of action
MTD, maximum tolerated dose
ORR, overall response rate
OS, overall survival
Q3W, every 3 weeks
Q4W, every 4 weeks
PBD, pyrrolobenzodiazepine
PFS, progression-free survival
PK, pharmacokinetics
PO, taken orally
PR, partial response
PS, performance status
RFS, relapse-free survival
R-GemOx, rituximab, gemcitabine, and oxaliplatin
RP2D, recommended Phase 2 dose
R/R, relapsed or refractory
SAE, serious adverse event
SD, stable disease
TEAE, treatment-emergent adverse event
WHO, World Health Organization

# LOTIS

## Learn more about the LOTIS Clinical Development Program

For additional outcome measures and inclusion/exclusion criteria, and a list of active study sites, visit www.ClinicalTrials.gov

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