LOTIS

Loncastuximab Tesirine Clinical Assessments

For information about the LOTIS Clinical Trial Program, visit www.adctmedical.com
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Loncastuximab tesirine (Lonca; loncastuximab tesirine-lpyl) 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 R/R 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).

Zynlonta has not received regulatory approval outside the United States.

Active LOTIS Clinical Trials

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 | **ACTIVE, NOT RECRUITING**

LOTIS-7

LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the safety and efficacy of loncastuximab tesirine in combination with other anticancer agents in patients with R/R B-NHL

NCT04970901 | **RECRUITING**

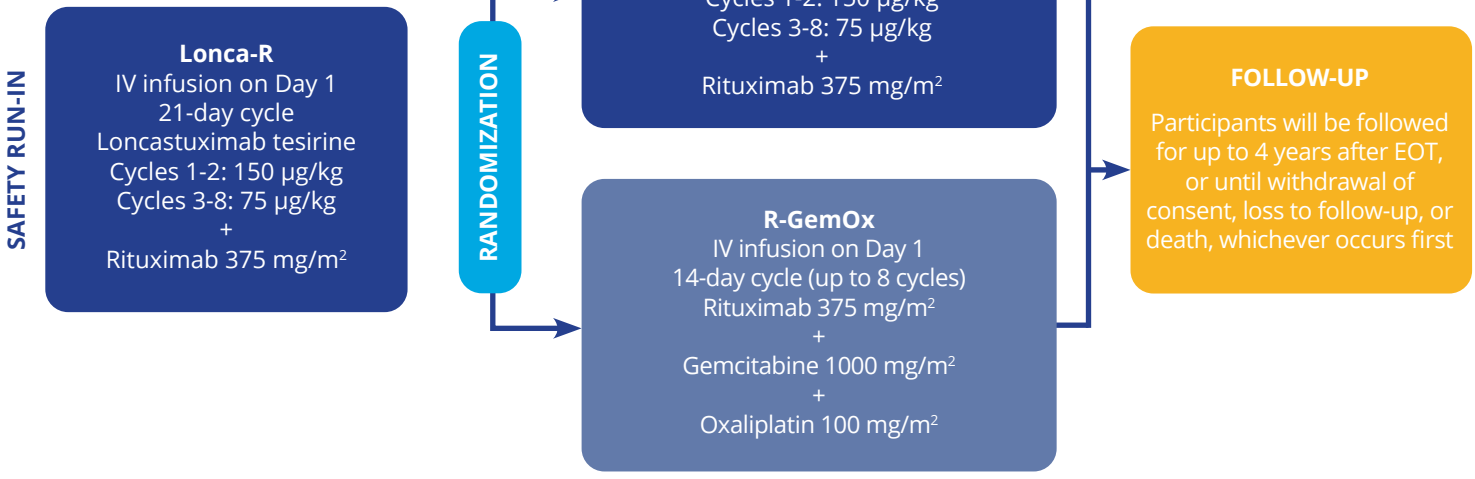
LOTIS-9

LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab in unfit/frail patients with previously untreated DLBCL

NCT05144009 | **RECRUITING**

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

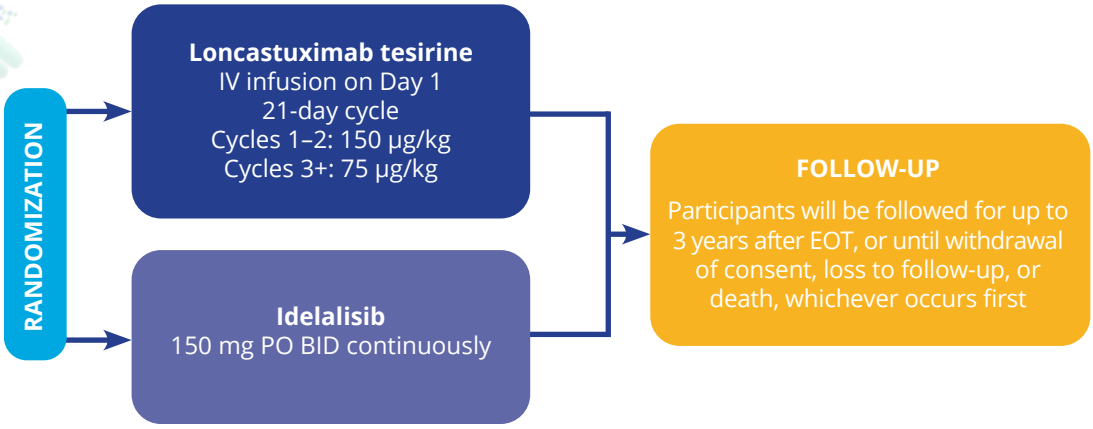
- ECOG PS 0 to 2
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, or high-grade B-cell lymphoma with *MYC* and *BCL-2* and/or *BCL-6* rearrangements
- R/R disease following ≥1 multi-agent systemic treatment regimens
- Lymphoma with active CNS involvement, including leptomeningeal 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 that has transformed to DLBCL or other aggressive lymphomas are not eligible
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- R/R 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

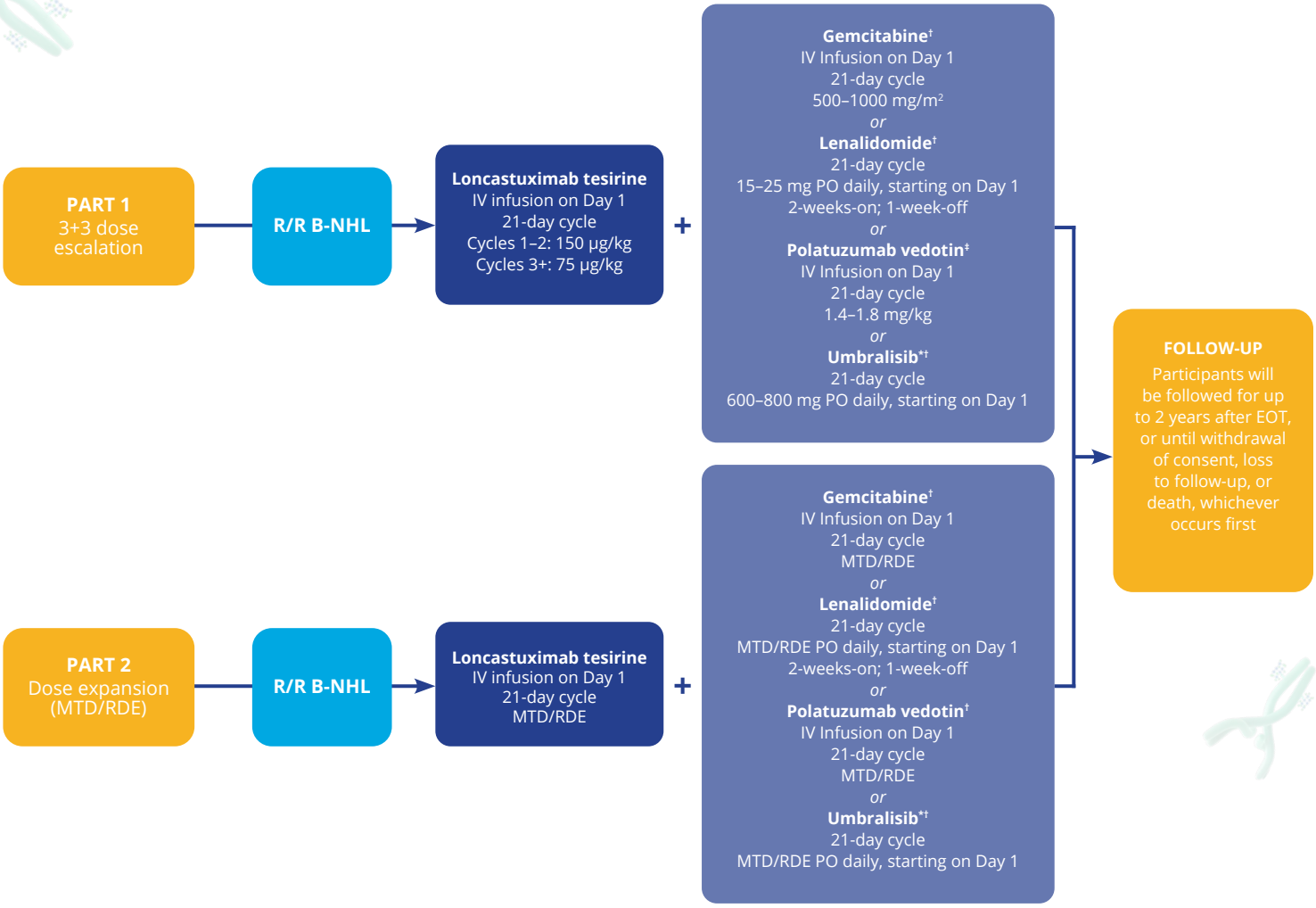
*According to the 2014 Lugano Classification.

LOTIS-6

LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the safety and efficacy of loncastuximab tesirine in combination with other anticancer agents in patients with R/R B-NHL

Part 1 (Dose Escalation): Loncastuximab Tesirine + Polatuzumab Vedotin Arm is the only arm currently enrolling.



KEY PRIMARY ENDPOINTS

- Number of participants who experience ≥1 TEAE and/or SAE; DLTs; AEs leading to dose delay, interruption or reduction

KEY SECONDARY ENDPOINTS

- ORR[§]
- DOR
- CRR[§]
- PFS
- RFS
- OS
- PK

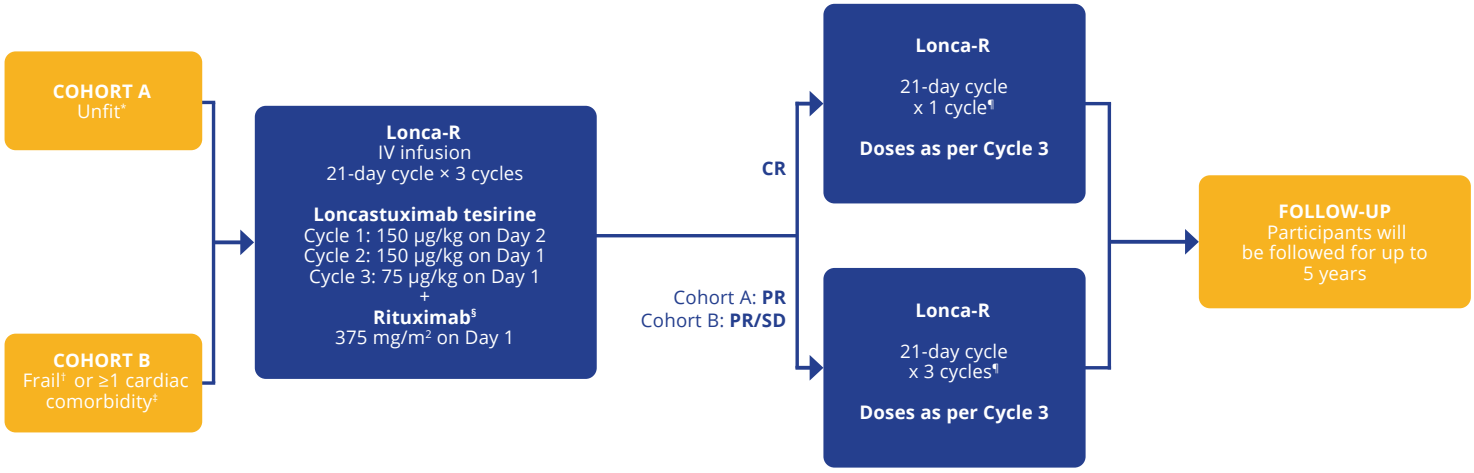
KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- Pathologic diagnosis of B-NHL, as defined by the 2016 WHO Classification (including DLBCL, HGBCL, FL, MCL, MZL, and BL)
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- R/R disease, have failed, or been intolerant to, any approved therapy, and have received ≥2 prior systemic treatment regimens
- AHCT or alloHCT permitted if received ≥60 days prior to start of study drug
- No prior loncastuximab tesirine, gemcitabine, lenalidomide, polatuzumab vedotin or umbralisib (applied to relevant arm and/or cohort of the specific drug administered)
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*Patients with a history of (or ongoing) inflammatory bowel disease, or confirmed CMV infection (CMV IgG-positive or IgM-positive and CMV DNA-positive) are not eligible for enrollment into this treatment arm.
†Not currently enrolling.
‡Currently enrolling.
§According to the 2014 Lugano Classification.

LOTIS·7
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2 open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab in unfit/frail patients with previously untreated DLBCL



KEY PRIMARY ENDPOINTS

- CR rate#; tolerability

KEY SECONDARY ENDPOINTS

- ORR#; 2-year
- PFS; 3-year
- OS;
- DOR; safety;
- HRQoL; pharmacokinetics; immunogenicity

KEY ELIGIBILITY CRITERIA

- Age ≥80 years or ≥65 years with ≥1 cardiac comorbidity‡
- Unfit* & Frail† patients as defined by sGA
- ECOG PS 0 to 2, or ECOG PS 3 if decline in status is deemed related to lymphoma and potentially reversible
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, HGBCL, or FL (Grade 3b)
- No prior therapy for DLBCL, HGBCL, or FL (Grade 3b)
- No prior loncastuximab tesirine or R-CHOP for any indication
- No prior treatment for aggressive lymphoma, except for up to 14 days of corticosteroids for symptom management

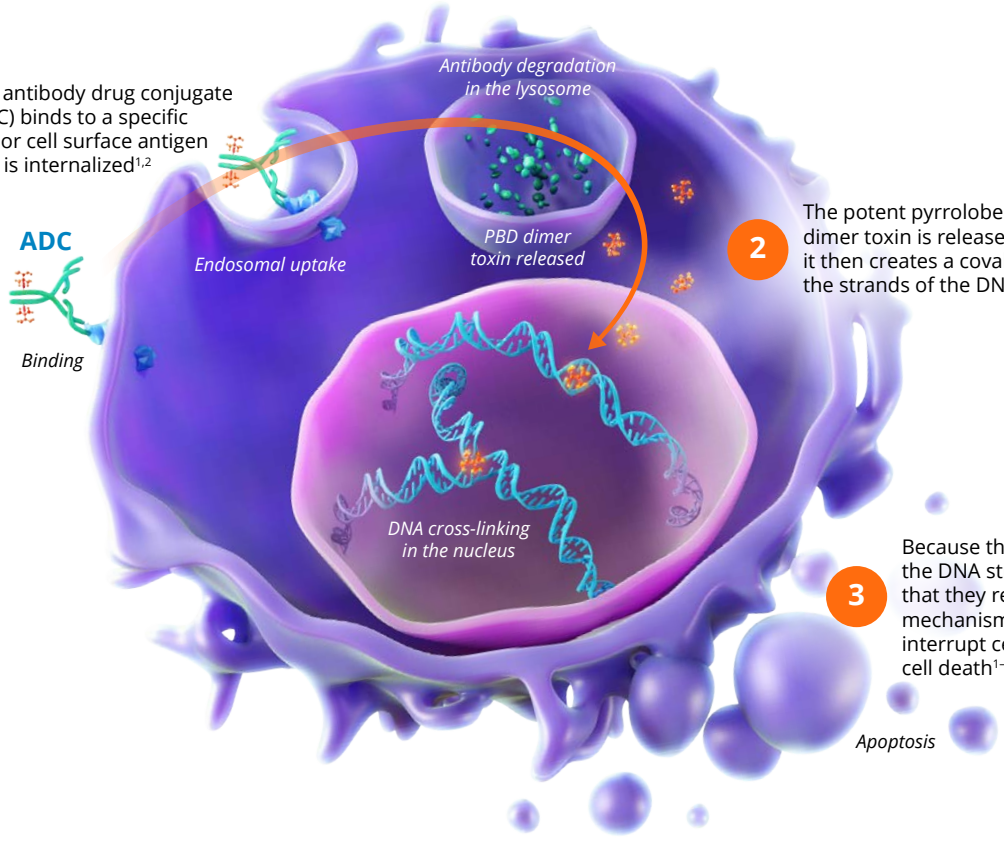
*Defined by the sGA as ≥80 years of age, an ADL score of 6, an IADL score of 8, and for CIRS-G: no score of 3-4 and <5 scores of 2 based on the FIL tool.
†Defined by the sGA as ≥80 years of age, an ADL score of <6, an IADL score of <8, and for CIRS-G: ≥1 score of 3-4 and ≥5 scores of 2 based on the FIL tool.
‡≥65 years of age with at least one of the following cardiac comorbidities: LVEF ≥30 to <50%; history of MI within 6 months prior to screening; IHD; history of stroke within 12 months prior to screening.
§A subcutaneous formulation of rituximab may be used at a flat dose of 1400 mg, starting from Cycle 2.
¶Up to 6 cycles may be administered per protocol.
#Responses according to the 2014 Lugano Classification.

LOTIS·9
LOncastuximab Tesirine ClinIcal AsSessment

ADC Therapeutics is advancing next-generation PBD-based ADCs

ADC Therapeutics is a commercial-stage biotechnology company dedicated to delivering next-generation PBD-based ADCs for those affected by cancer. With a deep understanding of ADC technology and of the oncology treatment landscape, ADC Therapeutics intends to address significant unmet medical needs and improve outcomes for those with difficult-to-treat cancers

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



1. The antibody drug conjugate (ADC) binds to a specific tumor cell surface antigen and is internalized[1,2]

2. The potent pyrrolobenzodiazepine (PBD) dimer toxin is released inside the cell, where it then creates a covalent cross-link between the strands of the DNA double helix[2,3]

3. Because these cross-links do not distort the DNA structure, it is hypothesized that they remain invisible to repair mechanisms and can covertly persist to interrupt cell division and cause tumor cell death[1–3]

LOTIS

LOncastuximab Tesirine ClinIcal AsSessment

Abbreviations

ADC, antibody drug conjugate
ADL, Activities of Daily Living
AE, adverse event
AHCT, autologous hematopoietic cell transplantation
AlloHCT, allogeneic hematopoietic cell transplantation
BID, twice daily
B-NHL, B-cell non-Hodgkin lymphoma
BL, Burkitt lymphoma
CD, cluster of differentiation
CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone
CIRS-G, Cumulative Illness Rating Scale-Geriatric
CMV, cytomegalovirus
CNS, central nervous system
CR, complete response
CRR, complete response rate
DLBCL, diffuse large B-cell lymphoma
DLT, dose-limiting toxicities
DOR, duration of response
ECOG PS, Eastern Cooperative Oncology Group performance status
EOT, end of treatment
FDA, US Food and Drug Administration
FIL, Fondazione Italiana Linformi
FL, follicular lymphoma
HGBCL, high grade B-cell lymphoma
HRQoL, health-related quality of life
IADL, Instrumental Activities of Daily Living
IgG, immunoglobulin G
IgM, immunoglobulin M
IHD, ischemic heart disease
IV, intravenous
Lonca-R, loncastuximab tesirine and rituximab
LVEF, left ventricular ejection fraction
MCL, mantle cell lymphoma
MI, myocardial infarction
MOA, mechanism of action
MTD, maximum tolerated dose
MZL, marginal zone lymphoma
ORR, overall response rate
OS, overall survival
PBD, pyrrolobenzodiazepine
PFS, progression-free survival
PK, pharmacokinetics
PO, taken orally
PR, partial response
R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
RDE, recommended dose for expansion
RFS, relapse-free survival
R-GemOx, rituximab, gemcitabine, and oxaliplatin
R/R, relapsed or refractory
SAE, serious adverse event
SD, stable disease
sGA, simplified geriatric assessment
TEAE, treatment-emergent adverse event
WHO, World Health Organization

References

1. Kaplon H, et al. mAbs. 2020;12:e1703531.
2. Zammarchi F, et al. Blood. 2018;131:1094–1105.
3. Hartley JA, et al. Sci Rep. 2018;8:10479.

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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

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

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