

LOR-2040

A novel RNA-targeted therapy being developed for the treatment of acute myeloid leukemia, high-grade myelodysplastic syndromes, bladder cancer and solid tumors.

MARKET OPPORTUNITY

- Significant unmet medical needs exist in oncology for:
 - Effective targeted therapies with utility in many cancers
 - Less toxic agents that can be combined with existing cytotoxic drugs for more tolerable and effective treatment
 - Effective salvage therapies for refractory and relapsed patients to overcome resistance

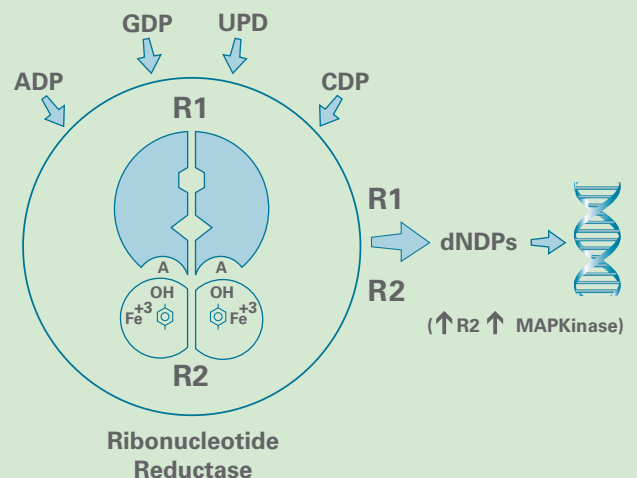
LOR-2040 has been designated Orphan Drug status for the treatment of AML by the U.S. FDA, providing seven years of market exclusivity in the U.S. upon the drug's approval for this indication.

LOR-2040 offers broad-spectrum activity in a variety of hematological and solid tumor diseases, representing considerable market potential.

Cancer indication	US incidence (2008)	LOR-2040 US Market Potential (USD)	LOR-2040 Global Market Potential (USD)
AML	13,290	140M	280M
MDS	11,540	101M	203M
Bladder	68,810	47M	94M
Prostate	186,320	1.2B	2.5B
NSCLC	166,675	4.7B	9.5B
Breast	184,450	7.2B	14.4B
Colorectal	148,810	2.7B	5.4B

MECHANISM OF ACTION

- LOR-2040 is a 20-mer antisense oligonucleotide that specifically targets the R2 subunit of ribonucleotide reductase (RNR), resulting in inhibition of DNA synthesis, cell division, and tumor growth.
- R2 is a highly regulated, cell cycle-controlled protein whose activity is required for DNA synthesis and repair.
- R2 has been identified as a genetic determinant that can profoundly alter the malignant potential of cancer cells.
- Elevated expression of R2 and RNR activity have been noted in a variety of primary tumors and tumor cell lines, and activation of the raf/ras/MAPK pathway can be induced through deregulated expression of the R2 RNR component.
- Overexpression of R2 increases the invasive potential of cancer cells. R2 expression can also determine tumor sensitivity to a variety of drugs with different modes of action.



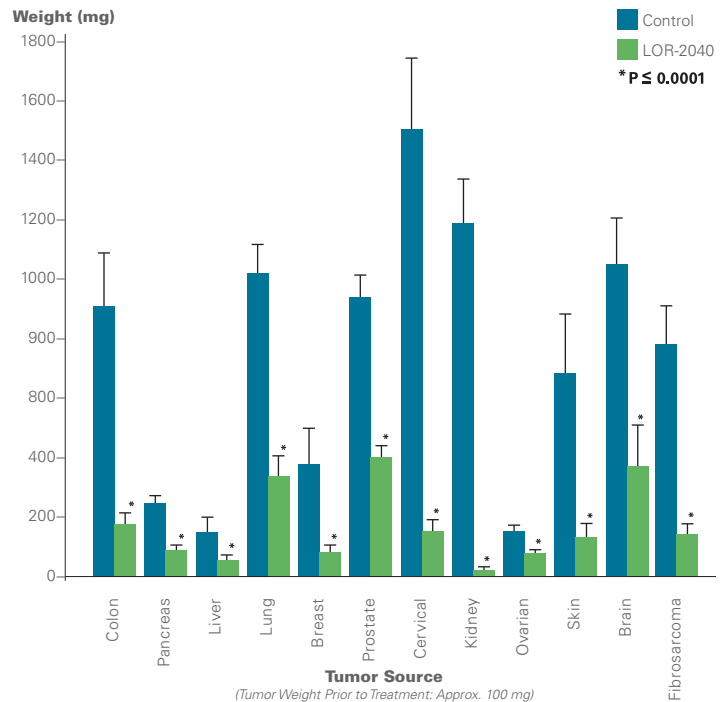
PRECLINICAL RESULTS:

- LOR-2040 has broad-spectrum activity in preclinical models, showing excellent antitumor efficacy.
- Antitumor activity of LOR-2040 is achieved at much lower doses than toxic dose, demonstrating a broad therapeutic window.
- Strong cooperative efficacy has been demonstrated preclinically with LOR-2040 in combination with a variety of chemotherapeutic regimens.
- Antimetastatic activity of LOR-2040 has been demonstrated in standard *in vivo* metastasis assays.
- Of importance to leukemia indications, LOR-2040 was highly effective in lymphoma and erythroleukemia survival models in mice in preventing almost all mortality, and this benefit was sustained in a discontinuation experiment even after the drug treatment was stopped.
- GLP-toxicology studies determined that LOR-2040 is well tolerated at doses up to 80 mg/kg in acute iv study in rhesus monkeys and at doses up to 50 mg/kg/day in 21-day repeat dose studies in rats and rhesus monkeys.
- Additional target validation studies conducted by Lorus using R2-specific siRNA showed that R2 downregulation correlated with dose-dependent antitumor activity in mouse models of renal cell carcinoma, and that specific knockdown of R2 expression resulted in antiproliferative activity and cell cycle arrest *in vitro*.
- The experimental evidence confirms that the antitumor activity of LOR-2040 is attributable to R2 target downregulation and not immunostimulatory factors.
- For further information, please refer to references 1 and 2.

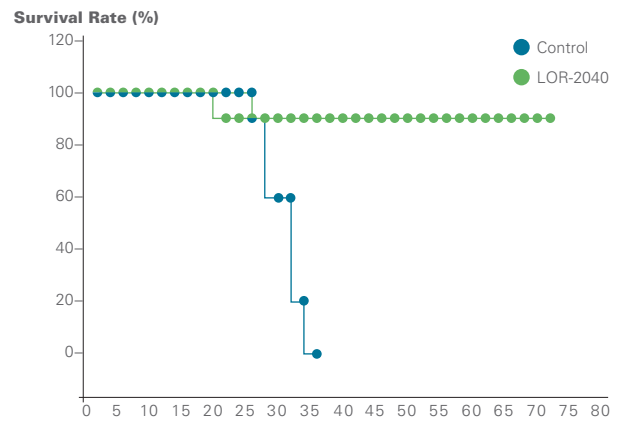
LOR-2040 CLINICAL DEVELOPMENT PROGRAM

- LOR-2040 development strategy in the clinic is focused primarily on combination administration with established chemotherapy due to strong cooperative activity seen preclinically, and the role of R2 downregulation in sensitizing many cancers to chemotherapy. Early clinical results have validated this strategy.
- Based on the target specificity and excellent single-agent tolerability of LOR-2040, it was anticipated that it would contribute minimal additional toxicity when added to many chemotherapy or immunotherapy regimens, while providing a more effective treatment opportunity.
- The following table summarizes all currently active clinical development programs with LOR-2040, including a number of studies sponsored by the U.S. National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP).

LOR-2040 PRECLINICAL EFFICACY IN VARIOUS HUMAN XENOGRAFT MODELS



SURVIVAL RATE OF CB-17 SCID MICE BEARING ERYTHROLEUKEMIA (CB7) TREATED WITH LOR-2040



(LOR-2040 and control were administered on Day 2 and continued on alternative days up to Day 71)

Current and Completed Trials

Cancer Indication
Acute Myeloid Leukemia (Refractory/Relapsed)
Acute Myeloid Leukemia (Refractory/Relapsed)
High-Grade Myelodysplastic Syndromes/Acute Leukemia
Bladder (Superficial and Non-Invasive)
Prostate
Non-Small Cell Lung
Breast
Colorectal
Solid Tumors
Renal Cell Carcinoma
Solid Tumors

CLINICAL RESULTS:

Acute Myeloid Leukemia Program:

• Phase Ib LOR-2040/high-dose cytarabine combination study in AML patients < 60 years of age with pharmacodynamic, dose ranging and efficacy objectives:

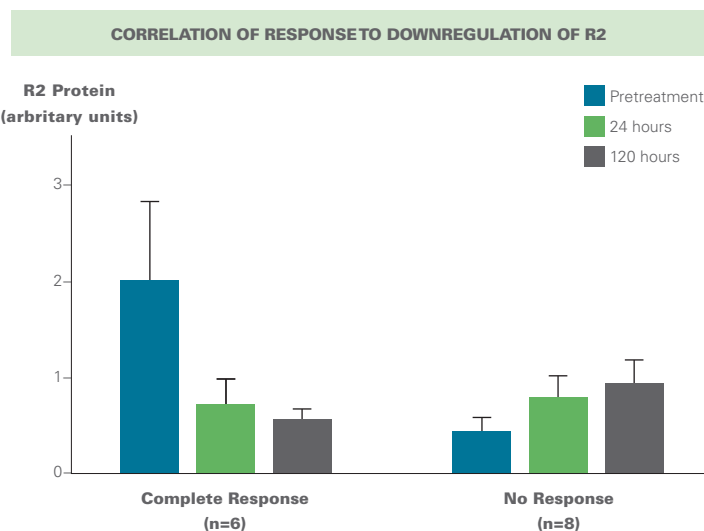
- This study evaluated a range of clinically active doses of this combination and established a 6 day course of 5 mg/kg LOR-2040 c.i.v. combined with cytarabine 3 g/m² twice daily for 4 of 5 days as the recommended Phase II dose.
- Favorable disease responses included complete responses in 8 (35%) of the 23 patients and significant cyto-reduction of leukemic blasts in 2 others. Seven of these 10 patients were further able to progress to a successful transplant, a desired outcome of successful salvage therapy. Notably, the study population included unfavorable patients with at least one adverse prognostic characteristic, in whom 50% were prior refractory and 50% relapsed in a median of <6 months.

Cancer indication	Pts <60 years (n=23)	Proceeded to Successful Allogeneic SCT
CR	8 (5 prior relapsed, 3 prior refractory*)	5
MRD	2 (cytoreduction to <10% BM blasts)	2

CR: Complete Remission; **MRD:** Minimal Residual Disease
 * Historically expected 2nd CR rate in refractory/relapsed (with <12 mo duration of 1st CR) is only 10-20% (Additionally some prior refractory patients had failed prior high dose cytarabine)

- Intracellular LOR-2040 levels were achieved within 24 hours:
 - Maintained over time with continuous infusion dosing in peripheral blood mononuclear cells (and for at least 2 days after end of dosing).
 - Increased to even higher levels over 5 days in bone marrow, suggesting accumulation in bone marrow.

- Changes in R2 protein level correlated with disease response:
 - R2 downregulation was seen in patients who achieved CR, and this downregulation occurred rapidly within 24 hours;
 - Pre-Treatment R2 levels were significantly higher in patients who eventually achieved CR;
 - Downregulation of R2 over 1 and 5 days in responding patients is shown below.



- Higher intracellular levels of LOR-2040 in more overtly leukemic CD34+ blasts correlate with more R2 downregulation
- Toxicities were comparable to those expected from high-dose cytarabine therapy alone and were not dose limiting.
- For further information, please refer to references 3 and 4.

Solid Tumor Programs:

- A series of 5 exploratory studies in various solid tumors, including colon cancer, breast cancer, non-small cell lung cancer (NSCLC) and hormone refractory prostate cancer were undertaken by the U.S. NCI-CTEP under a clinical trials agreement with Lorus following a review of prior preclinical and clinical data.
- Interim findings include: 47% with PSA response and only 7% with progression in combination with docetaxel and prednisone in hormone refractory prostate cancer; minor activity in combination with docetaxel in non-small cell lung cancer; preliminary evidence of R2 downregulation associated with clinical activity in combination with capecitabine in breast cancer. Further results will be reported on completion.
- Dose schedule optimization studies conducted in the laboratory by Lorus in parallel with the clinical program have shown strong schedule dependent synergy in support of further clinical development of this combination.
- For further information, please refer to references 5 - 7.

Combination Agent(s)	Status	Sponsor
Cytarabine	Phase II	Lorus
Cytarabine	Phase I	NCI
-	Phase I	NCI
-	PD Trial (Plan)	Lorus
Docetaxel/Prednisone	Phase II	NCI
Docetaxel	Phase I/II	NCI
Capecitabine	Phase II	NCI
Capecitabine/Oxaliplatin	Phase I	NCI
Gemcitabine	Phase I	NCI
Capecitabine	Phase I/II Completed	Lorus
-	Phase I Completed	Lorus

DEVELOPMENT STATUS - NEXT STEPS

• Acute Myeloid Leukemia Program:

- The ongoing Phase II study in relapsed/refractory AML is expected to proceed to interim evaluation of Stage 1 efficacy and evaluation of pharmacodynamic and pharmacokinetic predictors of combination activity in Q2 2009 with top-line results expected Q4 2009.
- This study aims to better explain the synergy achieved with the LOR-2040/high-dose cytarabine (HiDAC) combination, which is believed to be the result of sensitizing effect of LOR-2040 to cytarabine, as well as LOR-2040 overcoming the resistance that develops with multiple prior cytarabine-containing treatments over and above the expected direct contribution of each agent.
- In parallel with this program, additional research is under consideration to expand the efficacy experience to additional clinical practice environments in support of a multinational program.

• Myelodysplastic Syndrome Program:

- Lorus has undertaken, with U.S. NCI-CTEP sponsorship, a Phase I study of single-entity LOR-2040 in myelodysplastic syndrome (MDS) and related acute leukemias (AL). This ongoing study is intended to explore the opportunity for development of LOR-2040 in an MDS indication and for future potential combination with established first line drugs.

• Bladder Cancer Program (intravesicular route):

- Intravesicular administration of LOR-2040 has the potential advantage of directly targeting an accessible tumor in the bladder wall in order to achieve high local uptake by tumors without systemic effects.
- The preclinical program of LOR-2040 in support of the bladder cancer program was completed in Q3 2008
- This will be followed by regulatory submission of a pilot study of LOR-2040 as a single agent administered intravesically in patients with superficial and non-invasive bladder cancer in Q4 2008. Top-line results of this pilot study is anticipated in Q2/Q3 2009.

• Solid Tumor Programs:

- The Lorus program with LOR-2040 in solid tumors includes 5 studies sponsored by NCI-CTEP that are nearing completion. Future development in solid tumors will require selection of the best indication from the study programs in NSCLC, prostate cancer, breast cancer, colon cancer, and solid tumors, with various chemotherapies in combination with LOR-2040 and strategies for optimizing the combination dose schedule.

Partnering Status

Lorus Therapeutics is seeking partners who are interested in co-development and commercialization of LOR-2040 in the U.S., Europe and rest of the world.

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LOR-2040 - POINTS OF DIFFERENTIATION

• Excellent Target

- Validated (HU, siRNA and others) - loss of activity can not be compensated
- Highly over-expressed in cancer cells - modifies malignancy related pathways
- Cooperates with a variety of oncogenes to enhance cellular transformation and malignant potential

• Specific and selective anti-tumor agent

- Excellent antitumor efficacy in tumor growth, metastasis and survival assays in a broad range of cancers
- Strong efficacy in combination with standard therapeutic regimens

• Clinically relevant target down regulation

- Demonstrated in target and surrogate tissues

• Tumor stabilization and regression

- Demonstrated in renal, non-small cell lung, and breast cancer, and AML trials

• Favorable preclinical comparative data versus other antisense targets

- Highlights potential advantage of R2 target in multiple cancers

Intellectual Property

LOR-2040 is protected under several patents both for composition and cancer uses in a number of countries worldwide, including Canada, Europe, Australia, China, and the U.S. For more details, please visit our website at www.lorusthera.com.

References

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6. Juhasz A et al. Analysis of ribonucleotide reductase M2 mRNA levels in patient samples after GTI-2040 antisense drug treatment. *Oncol Rep.* 2006 May;15(5):1299-304.
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