

**Marqibo® — (Vincristine Optisome™)**

**A combination of modern nanoparticle technology and a potent, widely-used, cell cycle-specific chemotherapy**

Vincristine (VCR) is widely used in the treatment of leukemias, lymphomas, and multiple myeloma. Limited efficacy stems from cell cycle-specific (M-phase) activity combined with a short plasma half-life. Additionally, the dose is routinely capped at 2 mg due to peripheral neurotoxicity at the approved 1.4 mg/m<sup>2</sup> dose level. Marqibo® is VCR encapsulated in sphingomyelin and cholesterol nanoparticles called Optisomes™. Optosomal encapsulation facilitates VCR delivery at 2.25 mg/m<sup>2</sup> without dose-capping and provides the potential to overcome the limitations of conventional VCR.

**Optisomes represent a distinct technology uniquely geared towards improving chemotherapy efficacy and safety.**

Optisomes enhance penetration and retention of cell cycle-specific chemotherapies and have predictable drug release rates. Optisomes result in a 100-fold prolonged plasma circulating half-life of the encapsulated drug. Optisomes can preferentially exit the circulation from “leaky” tumor vasculature and accumulate in cancerous tissue, lymph nodes, bone marrow, and spleen. Extended and continuous drug exposure due to gradual drug release over several days results in a 5- to 15-fold increased intra-tumor drug exposure.

Improved PK	Targeted Delivery	Increased Concentration	Prolonged Exposure
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**Preclinical data demonstrates the value of Marqibo over VCR**

- 100-fold increased circulation time and plasma AUC
- Up to a 7.4-fold greater tissue (bone marrow, lymph node, implanted tumor, spleen, and liver) VCR exposure
- Increased therapeutic index in xenograft models compared to VCR unencapsulated or in other liposomes

**Clinical data demonstrate promising anti-cancer activity**

- 24% CR rate in relapsed/refractory adult ALL<sup>1</sup>
- 31% ORR in metastatic melanoma (25% CR in uveal subset)<sup>2</sup>
- 36% ORR in relapsed/refractory Hodgkin’s Disease<sup>3</sup>
- 93% CR rate in front-line aggressive NHL patients treated with R-CHMP (M = Marqibo)<sup>4</sup>
- 27% ORR in relapsed/refractory aggressive NHL<sup>5</sup>

<sup>1</sup>Thomas D et al. Blood 2007; 110 abstract 858; <sup>2</sup>Bedikian A et al. Melanoma Research (submitted); <sup>3</sup>Hana Biosciences, Inc., VSLI-05HD; <sup>4</sup>Rodriguez A et al. JCO 2004;22 abstract 8080; <sup>5</sup>Winter JN et al. Blood 2007 (submitted);



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# rALLY against Relapsed ALL

Now Recruiting—A study evaluating the efficacy and safety of weekly sphingomyelin/cholesterol-encapsulated vincristine nanoparticles (brand name Marqibo®)\* in patients with acute lymphoblastic leukemia (ALL) in second relapse

**Key study entry criteria:**

**Inclusion**

- Adults with Philadelphia chromosome negative ALL or lymphoblastic leukemia
  - Second relapse or
  - Failed 2 treatment lines of anti-leukemia chemotherapy
- Responsive to at least one prior anti-leukemia therapy, defined by a leukemia-free interval of >3 months
- ECOG performance status 0–3

**Exclusion**

- Burkitt’s lymphoma
- Active CNS disease

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