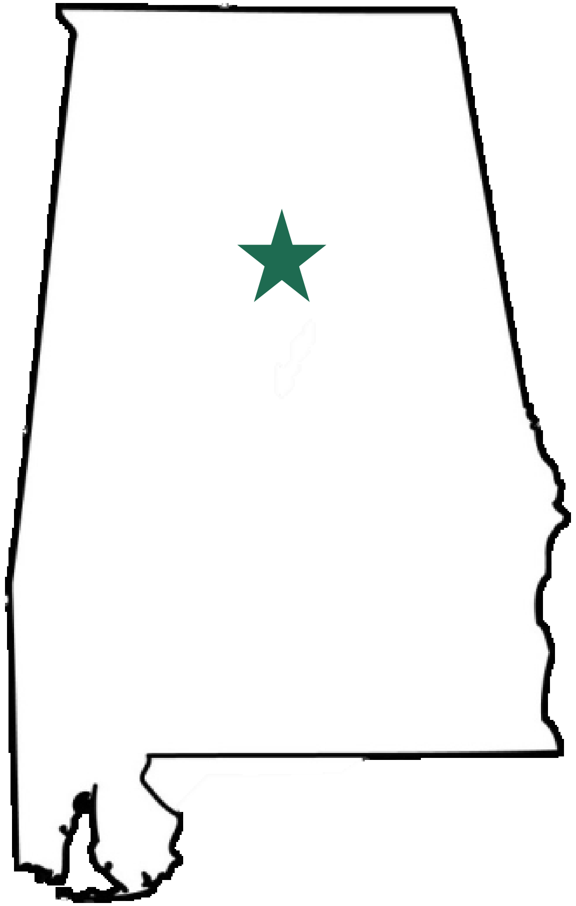
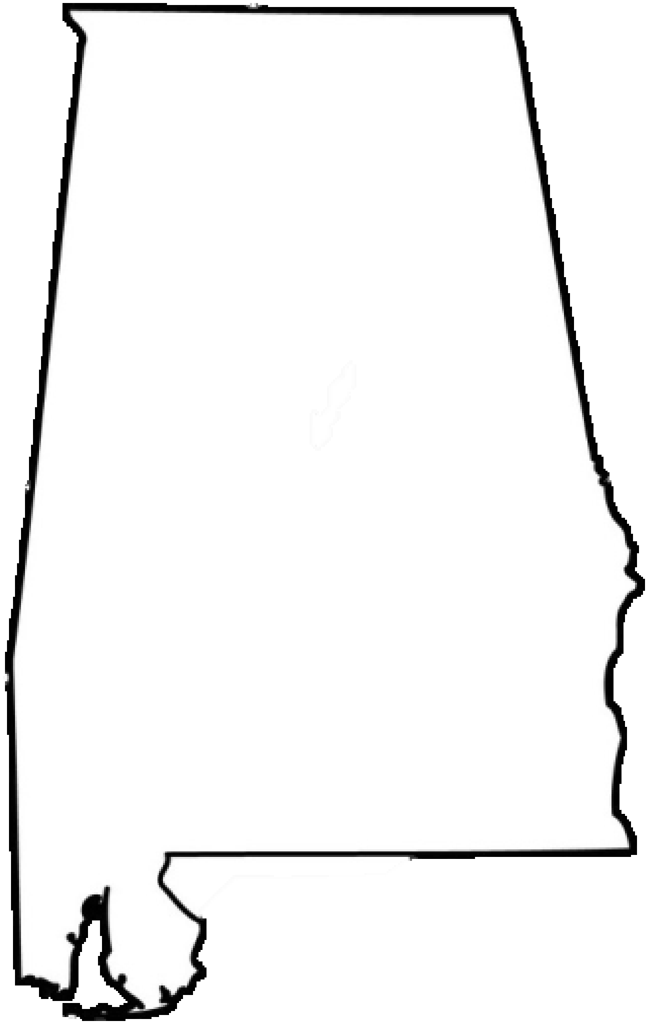
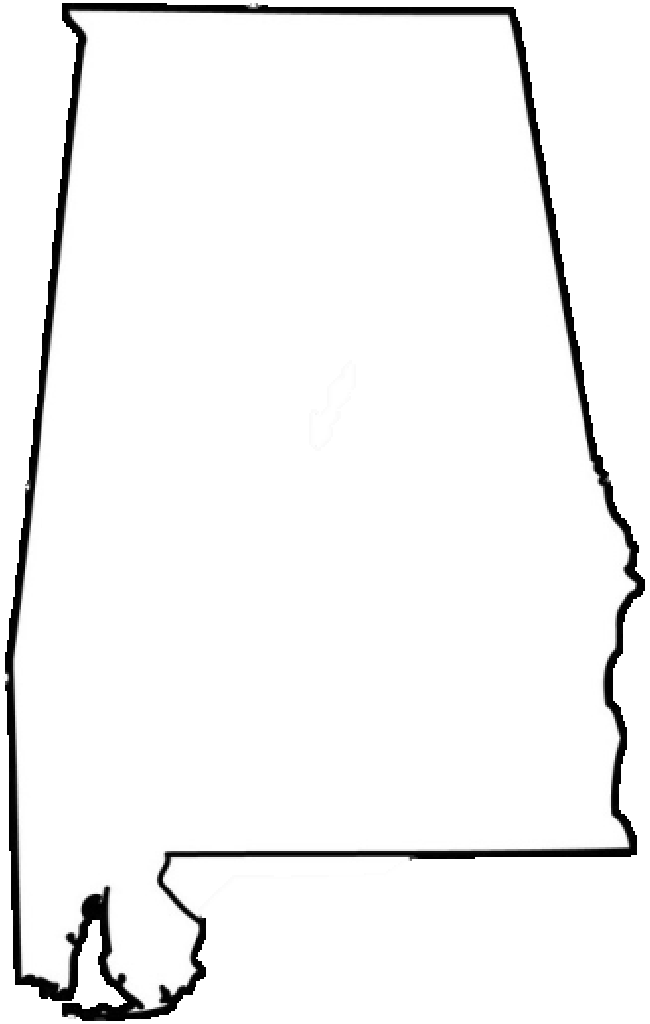
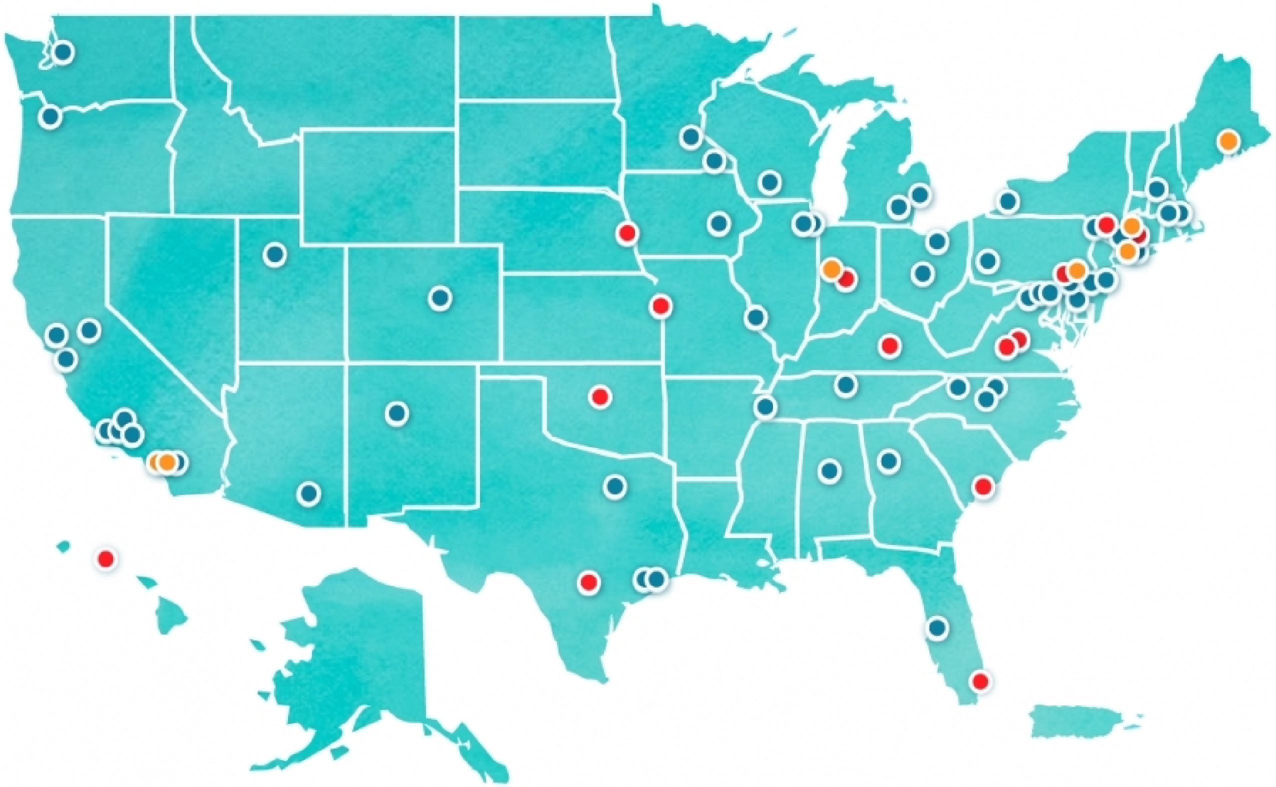
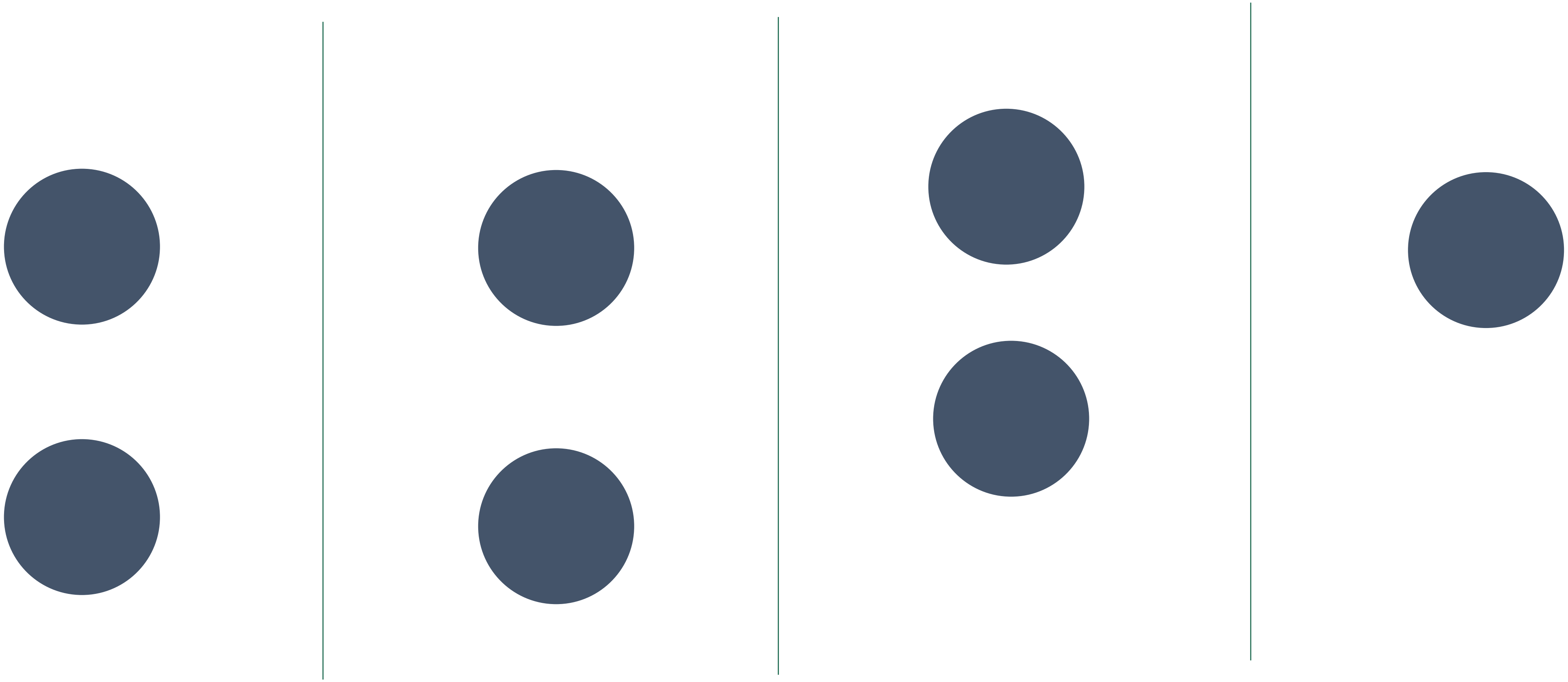


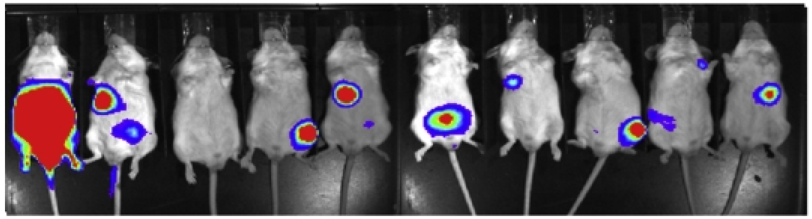


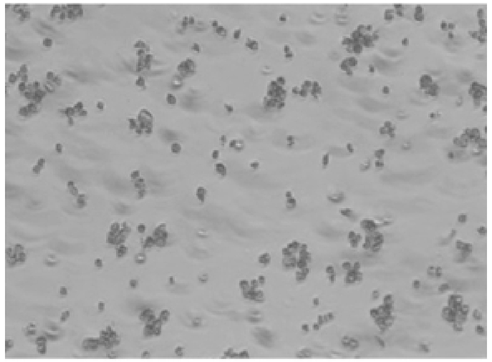


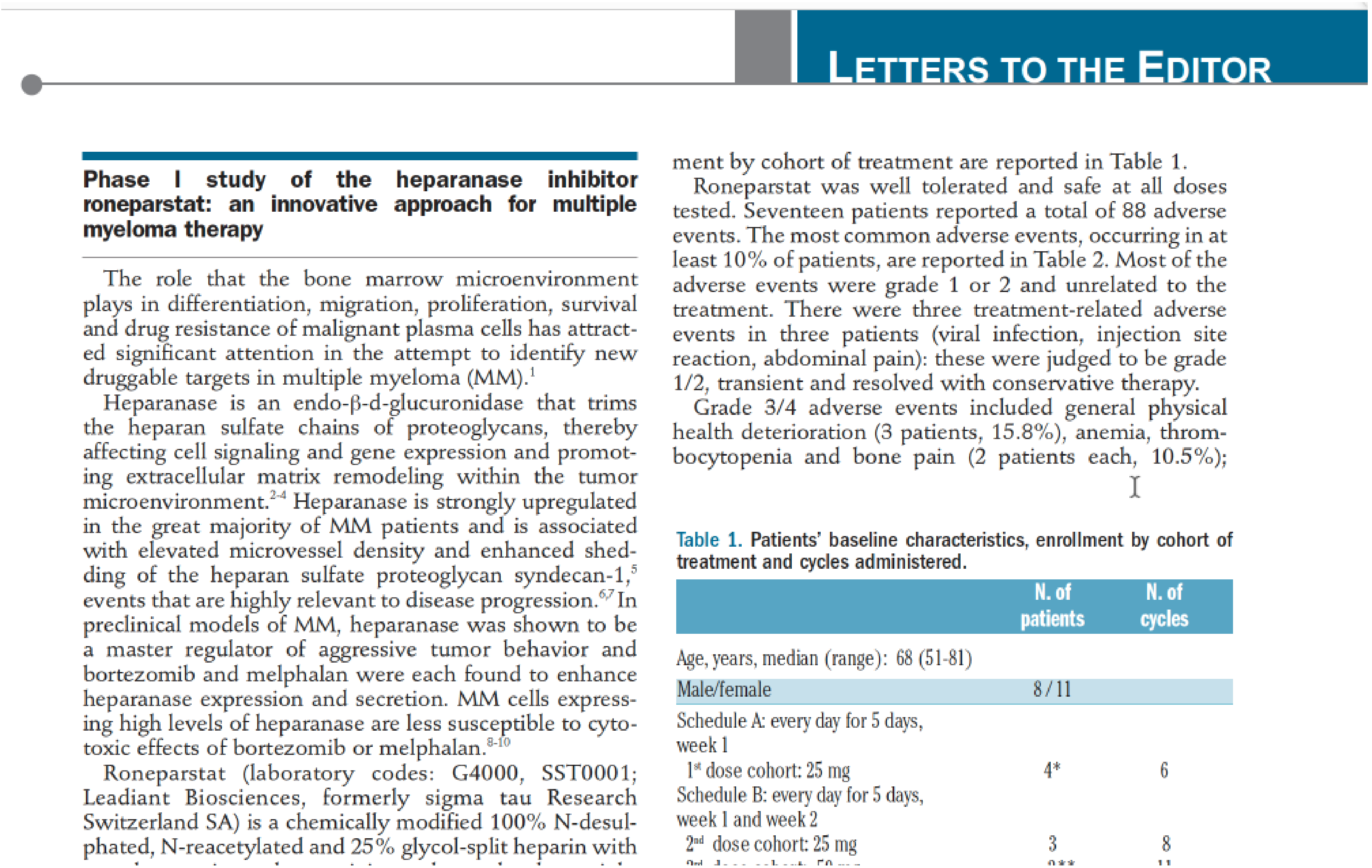


● CANCER CENTER ● COMPREHENSIVE CANCER CENTER ● BASIC LABORATORY









Phase I study of the heparanase inhibitor roneparstat: an innovative approach for multiple myeloma therapy

The role that the bone marrow microenvironment plays in differentiation, migration, proliferation, survival and drug resistance of malignant plasma cells has attracted significant attention in the attempt to identify new druggable targets in multiple myeloma (MM).[1]

Heparanase is an endo-β-d-glucuronidase that trims the heparan sulfate chains of proteoglycans, thereby affecting cell signaling and gene expression and promoting extracellular matrix remodeling within the tumor microenvironment.[2-4] Heparanase is strongly upregulated in the great majority of MM patients and is associated with elevated microvessel density and enhanced shedding of the heparan sulfate proteoglycan syndecan-1,[5] events that are highly relevant to disease progression.[6,7] In preclinical models of MM, heparanase was shown to be a master regulator of aggressive tumor behavior and bortezomib and melphalan were each found to enhance heparanase expression and secretion. MM cells expressing high levels of heparanase are less susceptible to cytotoxic effects of bortezomib or melphalan.[8-10]

Roneparstat (laboratory codes: G4000, SST0001; Leadiant Biosciences, formerly sigma tau Research Switzerland SA) is a chemically modified 100% N-desulphated, N-reacetylated and 25% glycol-split heparin with

ment by cohort of treatment are reported in Table 1.

Roneparstat was well tolerated and safe at all doses tested. Seventeen patients reported a total of 88 adverse events. The most common adverse events, occurring in at least 10% of patients, are reported in Table 2. Most of the adverse events were grade 1 or 2 and unrelated to the treatment. There were three treatment-related adverse events in three patients (viral infection, injection site reaction, abdominal pain): these were judged to be grade 1/2, transient and resolved with conservative therapy.

Grade 3/4 adverse events included general physical health deterioration (3 patients, 15.8%), anemia, thrombocytopenia and bone pain (2 patients each, 10.5%);

Table 1. Patients' baseline characteristics, enrollment by cohort of treatment and cycles administered.

	N. of patients	N. of cycles
Age, years, median (range): 68 (51-81)		
Male/female	8 / 11	
Schedule A: every day for 5 days, week 1		
1st dose cohort: 25 mg	4*	6
Schedule B: every day for 5 days, week 1 and week 2		
2nd dose cohort: 25 mg	3	8

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