

- The REMS program will consist of a communication plan to better educate patients and prescribers about the increased risk of occlusions and the revised indication. This will consist of letters to be mailed out to prescribing healthcare professionals informing them of the associated risks and a fact sheet and summary page also informing healthcare professionals about the risk to be distributed at meetings and disseminated through various medical journals. We note that the level of awareness will be evaluated by the FDA during its REMS assessment, which will be documented in the expected approval letter.
- There will be a number of PMRs, which, in our opinion, will better assess the true risk associated with Iclusig. Ariad will be held to four PMRs: 1) a pharmacovigilance assessment of risk factors associated with vascular occlusive events and an assessment of patient management and consequences with those who experience vascular occlusive events; 2) a prospective observation assessing the incidence of vascular occlusive events associated with Iclusig with or without anticoagulant or antiplatelet agents; 3) a follow-up of patients who were previously enrolled in the Phase I, II, and III (EPIC) studies to better understand the long-term safety of Iclusig; and 4) In the second half of 2014, a trial will be initiated to assess the long-term safety of Iclusig treatment, including the long-term risk of vascular occlusive events over time.