Debio 0932 is an oral second-generation heat shock protein 90 (HSP90) inhibitor, structurally unrelated to geldanamycin.

In the dose-escalation part of a Phase I study (NCT01168752), Debio 0932 mono-therapy has shown promising signs of efficacy in non-small-cell lung cancer (NSCLC).¹

Standard of care (SOC) for patients with advanced NSCLC, a good performance status, and no EGFR mutation, consists of doublet platinum-based chemotherapy (in combination with gemcitabine for squamous histology and in combination with pemetrexed for non-squamous histology).² ³ ⁴

In pre-clinical models, Debio 0932 has demonstrated additional efficacy in combination with SOC.

Further investigations into the potential role of Debio 0932 in combination with SOC for NSCLC are warranted.

**Objectives**

**Part A**: To determine the maximum tolerated dose of Debio 0932 in combination with cisplatin/pemetrexed and cisplatin/gemcitabine in treatment-naive patients with Stage IIIb or IV NSCLC and with docetaxel in previously treated patients with Stage IIIb or IV NSCLC.

**Part B**: To compare the effect of adding Debio 0932 to combination chemotherapy with cisplatin/pemetrexed and cisplatin/gemcitabine on the rate of progression-free survival (PFS) at 6 months in first-line therapy of patients with Stage IIIb or IV NSCLC.

**Part C**: To compare the effect of adding Debio 0932 to docetaxel on the change in tumor size in second-line therapy of patients with Stage IIIb or IV NSCLC.

**Study Design**

This study will include patients with advanced NSCLC (Stage IIIb or IV) without known EGFR mutation, and will consist of three parts:

**Part A** is an open-label dose escalation study of Debio 0932 in combination with SOC in patients who are candidates for first-line or second-line treatment. First-line SOC consists of cisplatin/gemcitabine in case of squamous histology and cisplatin/pemetrexed in case of non-squamous histology. Second-line SOC consists of docetaxel.

**Part B** is a randomized, double-blind, placebo-controlled study of Debio 0932 in combination with first-line SOC in 138 patients who did not receive previous systemic treatment for advanced NSCLC.

**Part B**: A sample size of 69 patients per treatment arm is required to detect a difference of 15% in the PFS rate at 6 months between the test arm Debio 0932 combined with dual chemotherapy (55%) and the control arm with placebo and dual chemotherapy (40%).

**Part C**: ≈ 70% of patients (N = 100) from Part B (first-line therapy) are expected to progress to Part C of the study (second-line therapy). These patients will be randomized into four treatment arms of about 25 patients, depending on whether they received Debio 0932 or placebo in Part B and will receive Debio 0932 or placebo in Part C.

Randomization will be stratified by squamous/non-squamous NSCLC, performance status 0 or 1, NSCLC Stage IIIb or IV, and KRAS status.

**Conclusion**

This international multi-center study will investigate the role of Debio 0932 in the first- and second-line treatment of advanced NSCLC. Study results are expected in 2014.