The phase II LAPACT trial of *nab*-paclitaxel (*nab*-P) plus gemcitabine (Gem) in patients with locally advanced pancreatic cancer (LAPC)

Philip Philip,[1] Scot Dowden,[2] Javier Sastre,[3] Venu Bathini,[4] Dana Cardin,[5] Jill Lacy,[6] Matthew Dugan,[7] Alberto Sobrero,[8] Charles Henderson,[9] Morton Coleman,[10] Edward Kim,[11] Wen Wee Ma,[12] Sheryl Koski,[13] Christophe Borg,[14] Giuseppe Tonini,[15] Fernando Rivera,[16] Louis Kayitalire,[17] Jack Shiansong Li,[17] Pascal Hammel[18]
[1]Karmanos Cancer Center, Detroit, MI; [2]Tom Baker Cancer Centre, Calgary, Alberta, Canada; [3]Hospital Clinico San Carlos, Madrid, Spain; [4]University of Massachusetts, Worcester, MA; [5]Vanderbilt Ingram Cancer Center, Nashville, TN; [6]Yale Cancer Center, New Haven, CT; [7]New England Cancer Specialists, Scarborough, ME; [8]Azienda Ospedaliera Universitaria San Martino, Genova, Italy; [9]Piedmont Cancer Institute, Atlanta, GA; [10]Clinical Research Alliance Inc, New York, NY; [11]UC Davis Comprehensive Cancer Center, Sacramento, CA; [12]Roswell Park Cancer Institute, Buffalo, NY; [13]Cross Cancer Institute, Edmonton, Alberta, Canada; [14]Centre Hospitalier Belfort Montbéliard, Montbéliard, France; [15]Policlinico Universitario Campus Biomedico Di Roma, Rome, Italy; [16]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain; [17]Celgene Corporation, Summit, NJ; [18]Hôpital Beaujon, Clichy, France

Background: Unresectable PC, which is characterized by a primary tumor that encases or abuts important regional blood vessels, is associated with a poor prognosis. Local (radiation or surgery) and systemic therapy options are available for patients with LAPC. A systemic therapy that induces substantial tumor shrinkage may improve local control of the disease and potentially increase survival. Gem is considered a standard of systemic therapy in LAPC. In the MPACT trial, *nab*-P + Gem demonstrated significantly greater efficacy than Gem alone in patients with metastatic PC, including the primary endpoint of overall survival (OS; median, 8.7 vs 6.6 months; HR 0.72; $P < 0.001$). An approximate 3-fold greater shrinkage of primary pancreatic tumors was also observed with *nab*-P + Gem vs Gem alone, suggesting the possibility of improved local PC control with *nab*-P + Gem. The LAPACT study will assess the efficacy and safety of first-line *nab*-P + Gem in LAPC.

Trial Design: This open-label, multicenter phase II trial (planned N ≈ 110) will enroll patients in the United States, Canada, and Europe. Patients with Eastern Cooperative Oncology Group performance status ≤ 1, histologically or cytologically confirmed unresectable LAPC, no distant metastases, and adequate organ function are eligible. Key exclusion criteria include histology other than adenocarcinoma, prior therapy for PC, any other malignancy within 5 years, peripheral neuropathy grade > 1, and clinically significant ascites. Eligible patients will receive *nab*-P 125 mg/m^2 plus Gem 1000 mg/m^2 on days 1, 8, and 15 of each 28-day cycle. Patients without disease progression or unacceptable toxicities after 6 cycles are eligible to receive an investigator's choice of surgery, chemoradiotherapy (Gem or capecitabine with radiation), or continuation of *nab*-P + Gem. Surgery may occur prior to completion of the planned 6 cycles of *nab*-P + Gem if a major response is observed. Patients will be followed until disease progression, withdrawal of consent, loss to follow-up, or death. The primary endpoint is time to treatment failure (TTF), defined as the time from the first dose of study therapy to discontinuation due to disease progression, start of a new non–protocol-defined anticancer therapy, or death. The study design allows for 80% power at a 1-sided alpha of 0.05 to detect a 30% increase in median

TTF compared with the 5.1-month median TTF observed for *nab*-P + Gem in the MPACT study. The secondary endpoints are disease control rate (DCR) after 6 cycles, overall response rate, progression-free survival, OS, safety, and health-related quality-of-life outcomes (as assessed by the European Organisation for Research and Treatment of Cancer questionnaires QLQ-C30 and QLQ-PAN26). As an exploratory endpoint, correlation of changes in circulating nucleic acids with disease progression and response to treatment will be evaluated. An interim analysis of DCR will occur after all patients have completed 6 cycles of *nab*-P + Gem, discontinued therapy due to disease progression, started a new non–protocol-defined therapy prior to completing 6 cycles of therapy, or died from any cause. Enrollment is ongoing (first patient was enrolled in April 2015). ClinicalTrials.gov identifier: NCT02301143.