Current Agreements

Dealdoc

Licensing and development agreement for PLX4032 (RG7204) in cancer therapy

Plexxikon
Roche

Oct 04 2006

Licensing and development agreement for PLX4032 (RG7204) in cancer therapy

Companies:	Plexxikon Roche
Announcement date:	Oct 04 2006
Related contracts:	Co-promotion and licensing agreement for PLX4032 (RG7204) for metastatic melanoma

Details

Announcement date:	Oct 04 2006
Industry sectors:	Bigpharma Bigbiotech Pharmaceutical
Therapy areas:	Research tools Oncology
Technology types:	Discovery tools Enabling technology Genomics Peptides Processes Small molecules
Deal components:	Co-promotion Development Licensing
Stages of development:	Preclinical

Financials

Milestones, US$m:	n/d : triggered by dosing of first patient in phase III trial n/d : development milestone payments of PLX4032
Royalty rates, %:	n/d : royalty payments on sales of PLX4032

Termsheet

4 October 2006

Plexxikon and Roche have entered into an agreement to develop and commercialize PLX4032.

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8 January 2010

Enrollment has been initiated and the first patient has been dosed in a Phase 3 trial of PLX4032 (RG7204) in patients with metastatic melanoma.

The initiation of the Phase 3 trial has triggered a significant milestone payment to Plexxikon from Roche.

Plexxikon also is entitled to receive additional payments for further milestone achievements as well as royalties on sales of PLX4032.

A Phase 2 trial (BRIM2) in previously treated melanoma patients was initiated in September 2009, with enrollment ongoing.

Press Release

Plexxikon and Roche Enter Partnership to Develop Targeted Cancer Therapeutic Medicine PLX4032

4 October 2006

Berkeley, California and Basel, Switzerland – 4th October, 2006 -- Plexxikon Inc. and Roche today announced they have entered into an agreement to develop and commercialize PLX4032, Plexxikon's investigational targeted cancer therapy which selectively inhibits B-RafV600E, a mutated form of the BRAF kinase gene. The BRAFV600E gene has been associated with increased tumor aggressiveness and decreased survival in many types of cancers and is a common cancer-causing kinase gene. The BRAFV600E gene is found in approximately 70% of malignant melanomas and a large number of colorectal and thyroid tumors. PLX4032 may offer a new treatment modality for the estimated 100,000 cancer patients in the United States who carry the BRAFV600E gene. Plexxikon recently filed an Investigational New Drug (IND) application for PLX4032 and plans to initiate a Phase 1 clinical trial by the end of this year.

Separately, Roche Molecular Diagnostics, a business unit of Roche Diagnostics, and Plexxikon announced they will collaborate on development of an in vitro assay to screen for the presence of the BRAFV600E mutation in biological samples taken from patient tumors. An assay that correlates the presence of this mutation with clinical outcome may aid clinical development of PLX4032.

"As one of the leading pharmaceutical companies in oncology, together with their commitment to personalized medicine, Roche makes an ideal partner for the development of this unique compound," said K. Peter Hirth, Ph.D., chief executive officer of Plexxikon Inc. "We believe PLX4032 could be a first-in-class oral cancer therapeutic which selectively targets an oncogenic protein found only in diseased tissue. Along with our Phase 2 diabetes product and preclinical stage portfolio in multiple therapeutic areas, PLX4032's entry into development further validates Plexxikon's discovery platform for novel drug candidates."

"There is a growing body of evidence demonstrating that agents such as PLX4032, which selectively inhibit activated kinases, are increasingly useful in treating cancer and improving patient outcomes," said Peter Hug, Roche's Global Head of Pharma Partnering. "We are very excited to partner with Plexxikon for the development of PLX4032 and other B-RafV600E targeted compounds. This could be a further example of the potential of personalized medicine. With our combined expertise in diagnostic and therapeutic development as well as commercialization, we are confident in our capability to develop this potential drug to make a difference to patients' lives."

Plexxikon Roche Collaboration

Under the terms of the agreement, Roche will pay Plexxikon $40 million as an upfront payment and a further $6 million in guaranteed research funding over the next two years. In addition, Plexxikon could potentially receive up to approximately $660 million over the term of the collaboration based on the successful completion of a series of development and commercial milestones for multiple indications and/or multiple compounds, as well as royalties on potential product sales.

Also under the collaboration, Roche and Plexxikon will jointly develop PLX4032 and follow on compounds targeting other BRAF kinase mutations. Plexxikon has filed an IND application for PLX4032, and will conduct a Phase 1 dose escalation study in patients with cancer, including melanomas. Roche will have a worldwide, exclusive license to develop and commercialize PLX4032, in addition to other anticancer compounds resulting from the partnership. Plexxikon retains the right to co-promote any product in the collaboration in the United States.

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1 June 2009

Plexxikon Announces PLX4032 Phase 1 Data Showing Objective Responses in Metastatic Melanoma Patients

ORLANDO, Florida and BERKELEY, Calif. - June 1, 2009 -- Plexxikon Inc. today announced preliminary data from a Phase 1 clinical study investigating PLX4032 (R7204). PLX4032 is a novel, oral and highly selective drug that targets the BRAFV600E cancer-causing mutation that occurs in most melanomas and about eight percent of all solid tumors. In patients whose cancer harbors this mutation and who were treated with therapeutic doses of PLX4032, tumor shrinkage and extended progression-free survival have been observed. Currently, two extension studies are being conducted in mutation-positive melanoma and colorectal cancer patients. Following the initial positive findings announced today, larger clinical trials to support a registration program for product approval are targeted to start later in 2009. Plexxikon and Roche are co-developing PLX4032 under their 2006 license and collaboration agreement.

"PLX4032 has shown both tumor shrinkage and delay in tumor progression in patients whose tumors harbor a BRAF mutation as well as reports of clinical symptom improvement in some patients," stated Keith T. Flaherty, M.D., assistant professor at the Abramson Cancer Center of the University of Pennsylvania and principal investigator for the PLX4032 Phase 1 clinical trial. "Seven years after BRAF mutations were first identified, we have validation that this mutation is a cancer driver and therapeutic target. This is a new and important chapter in the story of targeted therapy development in cancer, and we are especially excited for our melanoma patients, for whom there are currently few treatment options." Link to video clip of Dr. Flaherty

In the dose escalation phase of the study, 55 cancer patients have been treated, including 24 mutation-positive melanoma patients and 3 mutation-positive thyroid patients, as well as 28 melanoma, rectal and ovarian cancer patients who did not have the mutation or whose mutation status was not known.

In 16 BRAF mutation-positive melanoma patients treated with PLX4032 doses at or above 240 mg twice daily (BID), representing targeted drug exposure levels, data show:

PLX4032 is well tolerated at very high doses, with 960 mg BID under evaluation as the maximum tolerated dose

Partial responses in 9 patients showing greater than 30% tumor regression by RECIST (Response Evaluation Criteria in Solid Tumors) criteria, with 7 confirmed

Regression of metastatic lesions in every site to which melanoma commonly spreads, including liver, lung and bone

Minor responses in 4 patients showing tumor regression greater than 10% but less than 30%

Disease control lasting up to 14 months with continuous therapy, with many patients still receiving treatment

Interim median progression-free survival of at least six months, with many responding patients still receiving treatment

Dose-limiting toxicities, primarily rash, fatigue and joint pains, were seen at 1120 mg BID. Drug-related adverse events have been predominantly mild in severity and transient, including rash and photosensitivity. Serious adverse events were observed in some patients after chronic treatment, including possibly drug-related cutaneous squamous cell carcinoma. A risk management plan has been implemented for baseline evaluation of the skin and monitoring of all patients while on study. Cutaneous squamous cell carcinoma is typically excised by a patient's dermatologist.

"This is a significant day for us at Plexxikon. The clinical data for PLX4032 so far support our hypothesis that a truly selective drug can target tumors harboring this cancer-causing mutation, while at the same time, deliver a treatment that is well tolerated by patients," stated K. Peter Hirth, Ph.D., chief executive officer of Plexxikon. "In conjunction with bio-response markers and a companion diagnostic test, PLX4032 has all the hallmarks of an ideal personalized medicine. Plexxikon's pipeline includes several highly selective kinase inhibitors, including novel therapies for other cancers as well as other chronic diseases such as rheumatoid arthritis where such precision is anticipated to provide a safety advantage."

Companion Diagnostic in Parallel Development Along with the development of PLX4032 therapy, a diagnostic test to identify patients with the BRAF mutation is being co-developed by Plexxikon and Roche, under a separate 2005 agreement. This test is already being used to identify mutation-positive patients for ongoing clinical trials. Most importantly, this companion diagnostic enables the identification of mutation-positive cancer patients considered most likely to respond to PLX4032 treatment.

Exploring PLX4032 in Colorectal and Other Cancers The prevalence of the BRAF mutation is about eight percent of all solid tumors. Preclinical studies in colorectal cancer models also suggest that PLX4032 causes tumor regression, either as a single agent or in combination. Hence, future clinical trials may evaluate PLX4032 in tumor types beyond melanoma.

Currently, one of two extension cohorts is recruiting mutation-positive colorectal cancer patients in order to evaluate PLX4032 in this target population. In a retrospective study of 600 patients with colorectal cancer, including all stages and both genders, tumor tissue was tested for the presence of the BRAF mutation and correlated with outcomes. The data confirmed that approximately 10 percent of colorectal cancer patients carry this mutation, which is independent of the KRAS mutation, and those BRAF mutation-positive patients have a much poorer prognosis than patients with wild-type BRAF (ASCO 2009 Abstract #1103).

Additionally, in the Phase 1 dose escalation study which enrolled patients with several different tumor types, one mutation-positive thyroid patient showed a confirmed partial response, while two others showed stable disease with prolonged therapy.

Biomarkers Enhance Development of Personalized Medicine The development of PLX4032 has employed a variety of translational tools, including bio-response markers and an in vitro diagnostic test. These tools can potentially enable early detection of targeted pathway modulation and treatment response, as well as identification of the targeted patient population for this treatment.

Biomarker data from patient tumor biopsies before and after PLX4032 treatment showed early target modulation and when dosed at higher levels, have shown nearly complete inhibition of the desired target (ASCO 2009 Abstract #9021).

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8 January 2010

Plexxikon Announces First Patient Dosed In Phase 3 Trial Of PLX4032 (RG7204) For Metastatic Melanoma

Berkeley, CA—January 8, 2010 - Plexxikon Inc. announces that enrollment has been initiated and the first patient has been dosed in a pivotal Phase 3 trial of PLX4032 (RG7204) in patients with metastatic melanoma. PLX4032 is a novel, oral and highly targeted drug that is designed to inhibit the BRAF cancer-causingmutation that occurs in about 50 percent of melanomas and about eight percent of all solid tumors. The

randomized, controlled, Phase 3 “BRAFInhibitor in Melanoma” (BRIM3) trial in previously untreated patients is part of the planned registration program for PLX4032. The initiation of the Phase 3 trial has triggered a significant milestone payment to Plexxikon from Roche, its co-development partner, under their 2006 collaboration agreement. Plexxikon also is entitled to receive additional payments for further milestone achievements as well as royalties on sales of PLX4032. A Phase 2 trial (BRIM2) in previously treated melanoma patients was initiated in September 2009, with enrollment ongoing.

“With some tumor shrinkage in nearly all mutation-positive melanoma patients, and 70 percent of patients achieving at least 30 percent tumor shrinkage in our most recent clinical study, PLX4032 has shown meaningful anti-tumor activity. The Phase 3 trial, with a primary endpoint of overall survival, will provide an assessment of clinical benefit of PLX4032 in a randomized, controlled study design, which should further build our registration program for this drug,” stated K. Peter Hirth, Ph.D., chief executive officer of Plexxikon. “We are hopeful that this accelerated development program will enable us to bring this new personalized medicine to melanoma patients as quickly as possible. PLX4032 represents the first drug in Plexxikon’s promising franchise of oncology drug candidates.”

BRIM3 is a Phase 3 trial expected to enroll approximately 700 previously untreated melanoma patients who will be randomized one-to-one with PLX4032 at a dose of 960 mg BID or dacarbazine (DTIC), a comparator drug approved for the treatment of metastatic melanoma. Patients will be monitored throughout the study for safety and efficacy endpoints. The primary endpoint of this trial is overall survival. Secondary endpoints include duration of response, progression-free survival and best overall response rate (BORR). The BRIM3 trial is a multicenter study being conducted at approximately 100 sites, including sites in the United States, Australia, Europe and Canada, with sites continuing to open through Q2 2010.

BRIM2 is a Phase 2 trial expected to enroll approximately 100 patients and is a single-arm study in previously treated melanoma patients. This trial is enrolling patients at 13 sites in the U.S. and Australia.

Patients enrolling in both BRIM3 and BRIM2 are being selected using an investigational companion diagnostic test that detects the BRAF mutation. This diagnostic is being co-developed in parallel with PLX4032 by Roche Molecular Systems, Inc. and Plexxikon. Patients interested in enrolling in the BRIM2 or BRIM3 trials may find additional information at the Roche Clinical Trials Registry (http://www.roche-trials.com/), at genentechclinicaltrials@druginfo.com, by visiting www.clinicaltrials.gov, or by contacting the Roche/Genentech Call Center at 888-662-6728.

Filing Data

Not available.

Contract

Not available.