**PEGylated IL-10**

Pegilodecakin, LY3500518, AM0010
The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

Target
PEGylated interleukin-10 (IL-10) is a noncovalent homodimeric alpha-helical cytokine with structural similarities to interferon gamma (IFN-γ). PEGylated IL-10 promotes the expansion and activation of cytotoxic intratumoral CD8+ T cells, despite its known physiological anti-inflammatory properties. PEGylated IL-10 has demonstrated single-agent antitumor activity in preclinical tumor models, inducing CD8+ T-cell mediated tumor rejection of large, high-grade tumors in mice. Mice cured by PEG-murine IL-10 have a long-lasting immunity to the rejected tumor. PEGylated IL-10 combines preclinically and clinically well with chemotherapy and immune checkpoint inhibitors, including anti-PD-1.

Molecule
Pegilodecakin (LY3500518, AM0010) is a PEGylated form of recombinant human IL-10 (rHuIL-10). rHuIL-10 is a noncovalent homodimeric cytokine with an approximate monomeric MW of 18–19 kD and a dimeric MW of approximately 38 kD. AM0010 is derived from a human cDNA clone, recombinantly produced in E. coli and PEGylated at its N-terminus. Pegilodecakin is PEGylated at the N-terminal amino acid of one or both of the rHuIL-10 monomers with a 5 kD polyethylene glycol (PEG), resulting in an approximate 50%/50% mixture of mono- and di-PEGylated rHuIL-10. Pegilodecakin has been shown in vitro to increase the cytotoxic activity of CD8+ T cells.

Clinical Development
Pegilodecakin is being investigated in clinical trials in patients with pancreatic cancer or non-small cell lung cancer, and in a phase I clinical trial in early development.


* This clinical trial is being conducted globally.
† AM0010 is administered 5 µg/kg SQ on days 1-5 and 8-12.
‡ FOLFOX (leucovorin 400 mg/m² and oxaliplatin 85 mg/m² followed by bolus 5-FU 400 mg/m² and 46-hour infusion of 5-FU 2400 mg/m²) is administered intravenously on day 1 of a 14-day cycle until disease progression.

** Sequoia: A Randomized Study of AM0010 in Combination With FOLFOX Compared to FOLFOX Alone as Second-line Tx in Pts With Metastatic Cancer That Has Progressed During or Following a First-line Gemcitabine-Containing Regimen**

**Key Inclusion Criteria**
- Measurable adenocarcinoma
- Measurable disease defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Tumor progression during or following a gemcitabine-containing regimen on initial metastatic disease as established by CT scan or MRI
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Prior chemotherapy at least 2 weeks prior to randomization and recovered from toxicity to grade 1 or baseline

**Key Exclusion Criteria**
- Diagnosis of pancreatic islet neoplasm, acinar cell carcinoma, nonadenocarcinoma (ie, lymphoma, sarcoma), adenocarcinoma originating from the biliary tree, or cystadenocarcinoma
- Prior treatment with Coumadin and not willing to change to low molecular weight heparin or oral Factor II or Xa inhibitor with half-life < 24 hours
- Prior treatment with AM0010 or fluoropyrimidine/platinum-containing regimen
- Intolerant to a gemcitabine-containing regimen
- Prior history of HIV infection or active/reactivated hepatitis A, B, or C
- Prior irAEs of any grade or irAE requiring treatment for the treatment of advanced metastatic disease
- Prior treatment with a gemcitabine-based or any other chemotherapy in the activity’s activity
- Peripheral neuropathy or known history of diabetes or prodrug disposition
- Clinically significant bleeding within 6 weeks prior to randomization
- Diagnosis of bleeding disorder
- Prior history of immuno-related neurological disorders such as multiple sclerosis, chronic fatigue, or inflammatory or autoimmune disorders
- Clinically significant ascites defined as requiring paracentesis every 3 weeks
- Major surgery within 28 days prior to randomization or anticipated surgery during study period
- Prior history of treating immune modulation including, but not limited to, CTLA4, PD-1, and PD-L1
- Pregnant or breastfeeding
- Prior history of immune modulators including, but not limited to, CTLA4, PD-1, and PD-L1

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT02929291].

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**PEGylated IL-10**

| Pegilodecakin, LY3500518, AM0010 |

* This clinical trial is being conducted in the United States.
† AM0010 is dosed per body weight and administered SQ QD.
‡ Pembrolizumab is administered 200 mg intravenously over 30 min on day 1 of a 21-day cycle.

**Primary endpoint:** Objective response rate

**Key Inclusion Criteria**
- Metastatic or recurrent stage IV non-small cell lung cancer
- Tumor proportion score (TPS) ≥50%
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Measurable disease by CT or MRI scan as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Prior radiotherapy or radiosurgery completed at least 2 weeks prior to randomization
- No prior therapy for advanced disease. Previous neoadjuvant or adjuvant therapy is allowed for patients who successfully underwent complete radical surgery and ONLY if the last treatment was administered more than 6 months prior to the start of the trial treatment

**Key Exclusion Criteria**
- Active central nervous system metastases or carcinomatous meningitis
- Serious or uncontrolled medical disorder
- Active HIV or hepatitis infection
- Grade 1 toxicities as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 attributed to prior anticancer therapy (other than alopecia and fatigues) prior to randomization
- History of severe hypersensitivity reactions to monoclonal antibodies
- Pregnant or breastfeeding
- Prior use of an investigational agent within 28 days of first administration of trial treatment
- Prior therapy with antitumor vaccines or other immunostimulatory antitumor agents
- Prior therapy with anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, and/or anti-CTLA4 antibodies
- Nonsquamous NSCLC with known EGFR mutation or ALK rearrangement

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT03382899].

Cypress 1: A Randomized Phase 2 Trial of AM0010 in Combination With Pembrolizumab vs Pembrolizumab Alone as First-line (1L) Therapy in Patients With Stage IV/Metastatic Non-small Cell Lung Cancer and Tumors With High Expression of PD-L1 (>50%)*
The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

PEGylated IL-10 | Pegilodecakin, LY3500518, AM0010

* This clinical trial is being conducted in the United States.
† AM0010 is dosed per body weight and administered SQ QD.
‡ Nivolumab is administered 240 mg intravenously over 30 min on day 1 of a 14-day cycle.

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

Cypress 2: A Randomized Phase 2 Trial of AM0010 in Combination With Nivolumab vs Nivolumab Alone as Second-line Therapy in Subjects With Stage IV/ Metastatic Wild-Type Non-small Cell Lung Cancer and Low Tumor Expression of PD-L1

Primary endpoint: Objective response rate

Key Inclusion Criteria
- Metastatic or recurrent stage IV non-small cell lung cancer
- At least one prior systemic therapy that was not an anti-PD-1, anti-PD-L1, and/or anti-CTLA4 treatment for the metastatic disease (stage IV)
- Tumor proportion score (TPS) 0% to 49%
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Measurable disease by CT or MRI scan as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Completed prior radiotherapy or radiosurgery at least 2 weeks prior to randomization

Key Exclusion Criteria
- Active central nervous system metastases or carcinomatous meningitis
- Serious or uncontrolled medical disorder
- Active HIV or hepatitis infection
- > Grade 1 toxicities as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 attributed to prior anticancer therapy (other than alopecia and fatigue) prior to randomization
- Prior therapy with antitumor vaccines or other immunostimulatory antitumor agents
- History of severe hypersensitivity reactions to monoclonal antibodies
- Prior therapy with anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, and/or anti-CTLA4 antibodies
- Prior use of an investigational agent within 28 days of first administration of trial treatment
- Pregnant or breastfeeding

PLEASE VISIT www.clinicaltrials.gov FOR MORE INFORMATION ON THIS CLINICAL TRIAL (NCT03382912).
Active Trials Currently Not Enrolling

[NCT02009449] Early Development
Ivy: A Phase 1 Study of AM0010 in Patients With Advanced Solid Tumors

Pipeline information is current through April 30, 2019.

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