Copiktra™ (duvelisib) – New orphan drug approval

- On September 24, 2018, Verastem Oncology announced the FDA approval of Copiktra (duvelisib), for the treatment of adult patients with:
    - Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.
    - Relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies.
    - The FL indication was approved under accelerated approval based on overall response rate (ORR); continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- CLL and SLL are cancers that affect lymphocytes. There are approximately 200,000 patients in the U.S. affected by CLL/SLL with nearly 20,000 new diagnoses this year alone. While there are therapies currently available, real-world data reveals that a significant number of patients either relapse, become refractory, or are unable to tolerate current treatments.

- FL is typically a slow-growing or indolent form of non-Hodgkin lymphoma (NHL) that arises from B-lymphocytes. FL accounts for 20 to 30% of all NHL cases, with more than 140,000 people in the U.S. with FL and more than 13,000 newly diagnosed patients this year. FL is generally considered an incurable, chronic disease, with patients living for many years.

- Copiktra is an inhibitor of phosphoinositide 3-kinase (PI3K), and the first approved dual inhibitor of PI3K-delta and PI3K-gamma, two enzymes known to help support the growth and survival of malignant B-cells.

- The efficacy of Copiktra was demonstrated in an open-label study comparing Copiktra vs. Arzerra® (ofatumumab) in 319 adult patients with CLL or SLL. Efficacy was based on progression-free survival (PFS) in patients who had been treated with at least two prior lines of therapy.
    - Median PFS for Copiktra and Arzerra was 16.4 and 9.1 months, respectively (HR: 0.40).
    - The ORR was 78% for Copiktra vs. 39% for Arzerra.

- The efficacy of Copiktra was also evaluated in a single-arm study in 83 patients with FL who were refractory to Rituxan® (rituximab) and to either chemotherapy or radioimmunotherapy. Efficacy was based on ORR and duration of response (DOR).
    - The ORR was 42% (95% CI: 31, 54).
    - The DOR was 0 to 41.9 months.

- Copiktra carries a boxed warning for four fatal and serious toxicities, including: infections; diarrhea or colitis; cutaneous reactions; and pneumonitis.

- Additional warnings and precautions of Copiktra include hepatotoxicity, neutropenia, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Copiktra use were diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia.

- The recommended dose of Copiktra is 25 mg administered as oral capsules twice daily with or without food. A cycle consists of 28 days.

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    - The capsules should be swallowed whole. Patients should be advised not to open, break, or chew the capsules.
    - Prophylaxis for *Pneumocystis jirovecii* should be provided during treatment with Copiktra. Prophylactic antivirals to prevent cytomegalovirus (CMV) infection including CMV reactivation should also be considered during Copiktra treatment.

- Verastem Oncology plans to launch Copiktra immediately. Copiktra will be available as 15 and 25 mg capsules.