Drug development for advanced/metastatic, hormone-receptor (HR)-positive, human epidermal growth factor receptor-2 (HER2)-negative breast cancer has gained momentum in recent years. Following its approval in the United States and Europe in mid-2012 and approval in Japan in 2014, the mTOR inhibitor everolimus (Novartis’s Afinitor) in combination with exemestane (Pfizer’s Aromasin, generics) has rapidly become the sales-leading product for this therapy area. Furthermore, a first-in-class CDK4/6 inhibitor, Pfizer’s palbociclib (Ibrance) received FDA accelerated approval for first-line metastatic, HR-positive, HER2-negative breast cancer in combination with letrozole (Pfizer’s Femara, generics) in February 2015. The backbone of treatment in this population is hormonal therapies, most of which have suffered patent expiry; in addition, most patients in this population respond well to hormonal treatments, meaning improving efficacy with novel agents is difficult. Despite these challenges, the HR-positive, HER2-negative population holds the potential for significant commercial rewards for drug developers, given that it represents more than 70% of diagnosed incident cases of breast cancer.

Questions Answered in This Report:

- A drug’s performance on at least five efficacy end points, including median overall survival (MOS), progression-free survival (PFS), and overall response rate (ORR) are important for drug approval and oncologist prescribing. What are the key primary and secondary clinical trial end points with which new therapies are evaluated? How do U.S. and European oncologists weight specific efficacy end points and other drug attributes in their prescribing decisions for advanced/metastatic, HR-positive, HER2-negative breast cancer?

- Increased overall survival (OS), improved time to disease progression, and improved tumor response are key areas of unmet need for advanced/metastatic, HR-positive, HER2-negative breast cancer according to the insights of surveyed U.S. and European oncologists. Which therapies in development for advanced/metastatic, HR-positive, HER2-negative breast cancer are poised to fulfill these needs? What clinical and/or regulatory challenges must drug developers overcome in order to capitalize on these areas of unmet need? What degree of improvement over currently available therapies do surveyed U.S. MCO PDs seek from new therapies on key clinical attributes for which surveyed physicians indicate there is high unmet need?
- Median PFS and incidence of high-grade neutropenia are key drivers of physicians’ prescribing decisions and/or are the focus of drug development for new advanced/metastatic, HR-positive, HER2-negative breast cancer therapies. What trade-offs across these and other clinical attributes are U.S. oncologists willing to make when considering the use of emerging therapies for the treatment of advanced/metastatic, HR-positive, HER2-negative breast cancer? Based on the trade-offs in price and performance across key drug attributes that U.S. oncologists are willing to make, how do physician preference and prescribing likelihood vary across different target product profiles for advanced/metastatic, HR-positive, HER2-negative breast cancer?

- By 2018, palbociclib + letrozole will emerge as the gold-standard therapy in our Drug Comparator Model because of its superior clinical profile over the key current therapies we evaluated. On what clinical attributes is palbociclib most differentiated from its competitors? Which current therapies are at greatest risk of being replaced by palbociclib? Are any other emerging therapies poised to compete with palbociclib for gold-standard status?

Scope:
Attributes included in conjoint analysis-based assessment of target product profiles for advanced/metastatic, HR-positive, HER2-negative breast cancer:
- Median overall survival (months)
- Progression-free survival (months)
- Overall response rate (% of patients)
- All grades stomatitis (% of patients)
- Grade 3/4 neutropenia (% of patients)
- All grades fatigue (% of patients)
- Price per 28-day cycle

Attributes included in assessment of U.S. payers’ receptivity to new therapies for advanced/metastatic, HR-positive, HER2-negative breast cancer:
- Effect on overall survival
- Effect on progression-free survival
- Incidence of grade 3/4 neutropenia
- Incidence of fatigue (all grades)

Physicians surveyed: 60 U.S. and 30 European oncologists.
Payers surveyed: 20 U.S. MCO PDs.

Comprehensive List of Therapies Included in Our Research and Modeling:
Current Therapies
- Everolimus + exemestane (Novartis’s Afinitor + Pfizer’s Aromasin, generics)
- Letrozole (Novartis’s Femara, generics)
- Exemestane (Pfizer’s Aromasin, generics)
- Fulvestrant (AstraZeneca’s Faslodex)
- Docetaxel (Sanofi’s Taxotere, generics)

**Emerging Therapies**

- Palbociclib + letrozole (Pfizer’s Ibrance + Novartis’s Femara, generics)
- Abemaciclib + fulvesrant (Eli Lilly + AstraZeneca’s Faslodex)
- Buparlisib + fulvesrant (Novartis + AstraZeneca’s Faslodex)
- Entinostat + exemestane (Syndax Pharmaceuticals + Pfizer’s Aromasin, generics)
- Enzalutamide + exemestane (Astellas Pharma/Medivation’s Xtandi + Pfizer’s Aromasin, generics)

**Report Details**

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