Career Development Series 2022

Developing Regulatory Strategies for Your Novel Drug or Device

Presentation will begin at 12:00 PM (PT)

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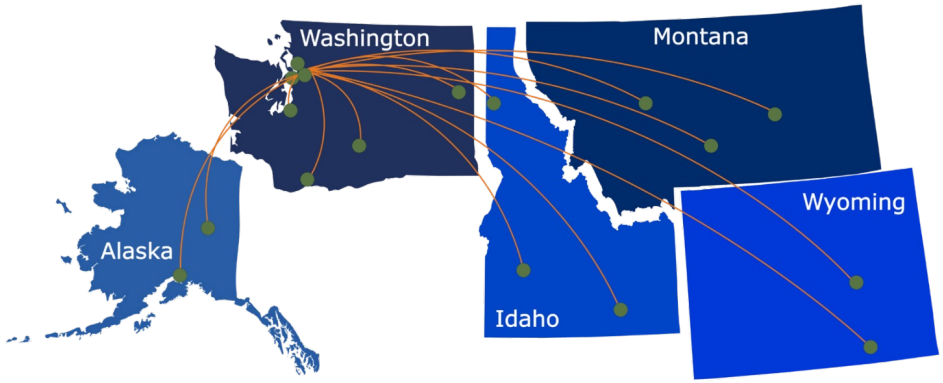

What We Offer:

1. **Research Support Services:** Members gain access to the different research services, resources, and tools offered by ITHS, including the ITHS Research Navigator.

2. **Community Engagement:** Members can connect with regional and community based practice networks

3. **Education & Training:** Members can access a variety of workforce development and mentoring programs and apply for formal training programs.

4. **Funding:** Members can apply for local and national pilot grants and other funding opportunities. ITHS also offers letters of support for grant submissions.

Contact ITHS

Director of Research Development

- Project Consultation
- Strategic Direction
- Resources and Networking

Melissa D. Vaught, Ph.D.
ithsnav@uw.edu
206.616.3875

Scientific Success Committee

- Clinical Trials Consulting
- Guidance on Study Design, Approach and Implementation
- Feedback on Design and Feasibility

https://www.iths.org/investigators/services/clinical-trials-consulting/

Upcoming Career Development Series 2022

Sept. 27th – How to be an Amazing Reviewer

Oct. 3rd – When and How to Say No with Confidence:
Aligning commitments with professional goals and interests

Oct. 6th – Introduction to the Team Science Seminar Series 2022-2023:
Why is Team Science Important?

Nov. 3rd – Team Science CDS – Topic TBC

Dec. 7th – Biosketch 101: Getting (Grant Reviewers) to Know You

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Feedback

At the end of the seminar, a link to the feedback survey will be sent to the email address you used to register.

Career Development Series 2022

Developing Regulatory Strategies for Your Novel Drug or Device

Presented by:
Lynn M. Rose, Ph.D.
Affiliate Associate Professor School of Pharmacy
Institute of Translational Health Sciences

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Learning Objectives

At the end of the session, participants will be able to:

1. Understand the dependence of the regulatory strategy on the clinical indication
2. Understand the complexities involved in defining the clinical indication for a development program
3. Identify relevant ‘regulatory precedent’ to help guide development programs for drugs and devices
4. Be better prepared to conduct a Regulatory Assessment for your own product

OVERVIEW

1. Review Definitions of Clinical Indications
2. Use Product Labels as Guide to Planning
3. Regulatory Review Pathways
4. Where to Find Information Relevant to Regulatory Plan

What is a Clinical Indication?

Ultimately, a new treatment is characterized by its "**indication**." An ideal treatment **indication** will consist of a disease, a patient population, an intervention, and an outcome.

[*National Research Council (US) Panel on Handling Missing Data in Clinical Trials.]*

The Disease

- The exact medical definition of “disease” can range from primarily signs and symptoms (e.g., headache, pneumonia) to presumed causative agents (e.g., pneumococcal pneumonia).

- Other times, the lack of efficacy of the usual treatment is incorporated into the definition of the disease (multidrug resistant *Staph aureus*).

- In some cases the description of the disease may include the method of diagnosis (e.g., culture positive gram negative septicemia).

The Population

- A treatment might be indicated only for a subpopulation of patients who satisfy the diagnostic criteria for the disease (e.g. Stage II-III adenocarcinoma).

- An indication for a new treatment might be for patients for whom the standard therapy has failed or is inadvisable due to a concurrent medical conditions (e.g., pediatrics, pregnancy, poor renal function).

The Intervention

- An intervention consists of a specific formulation of the drug(s), a mode of administration, the dosing strategy, auxiliary treatments, and the duration of treatment.
- Some treatments are combinations of drugs, either in a common formulation or administered separately.
- A mode of administration can include topical, oral, subcutaneous, intramuscular, or intravenous.
- The dose may be specified as a common level to be used by all individuals or as a dose specific to patient body size or body surface area.
- The dosing strategy might include a gradual increase in dose as treatment is initiated, a tapering of dose as the patient is weaned from the therapy.

The Outcome

- The intended outcome of a treatment is typically characterized clinically, as outcomes that materially affect the course of the disease (e.g., lower risk of mortality, relief of symptoms, improvement in quality of life).

- In some settings, a strong risk factor thought to represent a surrogate outcome measure of subclinical disease or disease risk will be used (e.g., hypertension).

- The precise definition of the outcome might explicitly include the time frame of measurement (e.g., postprandial serum glucose levels) and the method of measurement (e.g., decreasing serum glucose levels as reflected in Hemoglobin A1c), or the time frame.

Indications and Usage in Product Label

————INDICATIONS AND USAGE————

TECENTRIQ is a programmed death-ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with:

Locally advanced or metastatic urothelial carcinoma who:

- are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area), as determined by an FDA-approved test, or
- are not eligible for any platinum-containing chemotherapy regardless of PD-L1status, or
- have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy. (1.1)
- This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.1)

Metastatic non-small cell lung cancer who have disease progression during or following platinum-containing chemotherapy.

Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving TECENTRIQ. (1.2)

Examples Including Concomitant Therapy

1 INDICATIONS AND USAGE

DRUG-X is **indicated in combination with an aromatase inhibitor as initial endocrine-based therapy** for the treatment of **postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.**

1 INDICATIONS AND USAGE

DRUG-X is indicated for the treatment of carcinoid syndrome diarrhea **in combination with somatostatin analog (SSA) therapy** in **adults inadequately controlled by SSA therapy.**

Examples Including Specific Tests

1 INDICATIONS AND USAGE

1.1 Acute Myeloid Leukemia

DRUG-X is indicated for the treatment of adult patients **with relapsed or refractory** acute myeloid leukemia (AML) **with an isocitratedehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.**

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of AML with DRUG-X **based on the presence of IDH2 mutations in the blood or bone marrow** [see Indications and Usage (1.1) and Clinical Studies (14.1)]. Information on FDA-approved tests for the detection of IDH2 mutations in AML is available at http://www.fda.gov/CompanionDiagnostics.

Other Factors Impacting Clinical Indication

- How many Competitor Products in Development?
  - Will you be able to enroll a sufficient number of subjects?
  - Do you have Key Opinion Leaders supporting you?
- The Broader the Indication (e.g., all bladder cancer)
  - The greater the market potential 
  - Heterogeneity among patient population = lack of clear study outcome
  - Not financially viable
  - Could decrease regulatory options 
- The Narrower the Indication (e.g., bladder cancer failed cisplatin)
  - Clear trial endpoint
  - Increase access to acceleration pathways 
  - Harder to find subjects for clinical trials
  - The smaller the market share
  - No data to extend to larger population 

FDA Review Categories can Influence Choice of Indication

Mechanism	Description
Fast-Track	Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
Breakthrough Designation	A process designed to expedite the development and review of drugs which may demonstrate substantial improvement over available therapy.
Accelerated Approval	These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.
Priority Review	A Priority Review designation means FDA's goal is to take action on an application within 6 months

FDA Review Categories can Influence Choice of Indication

Mechanism	Description
Orphan Drug Designation	The Orphan Drug Act provides financial incentives to those drugs and biologics designated as orphan drugs. To qualify, these products must be intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S
Emergency Use Authorization	Allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats including infectious diseases, by facilitating the availability and use of medical countermeasures (MCMs) needed during public health emergencies.
Humanitarian Use Device	A Humanitarian Use Device (HUD) is a "medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year."

Other Impacts Related to Clinical Indication

- Definition of the **nonclinical studies** to be conducted (species, duration of exposure)
- Manufacturing goals (scale-up, material costs)
- Clinical Trial Design – complexity = cost
- Future reimbursement by insurance (unmet medical need)
- Market Potential (competition)
- Regulatory Review Options

Where to Look for Information?

- Is a product with a similar “mechanism of action” already marketed as a drug in the US? Is it marketed elsewhere in the world?
- Are there different drugs approved for the clinical indication you are interested in?
  - Code of Federal Regulations (CFR)
  - FDA Website: http://www.accessdata.fda.gov/scripts/cder/drugsatfde
  - Labels of Related Products
  - Google: www.google.com

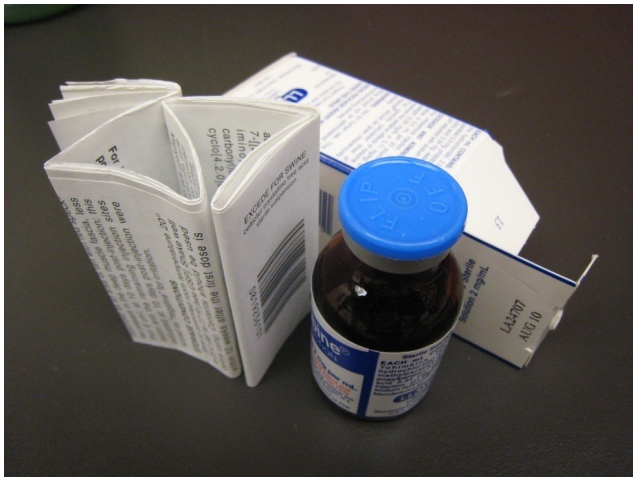
Where to Look for Information?

- Information about other potential uses of the drug (*Label, PubMed, Company Website*)
- Information about the safety of **similar** compounds or animal models conducted to support an indication (*patent applications, scientific literature*)
- Assess currently ongoing studies with competitor products or the same indication (*ClinicalTrials.gov*)
- Assess FDA requirements for nonclinical and regulatory components

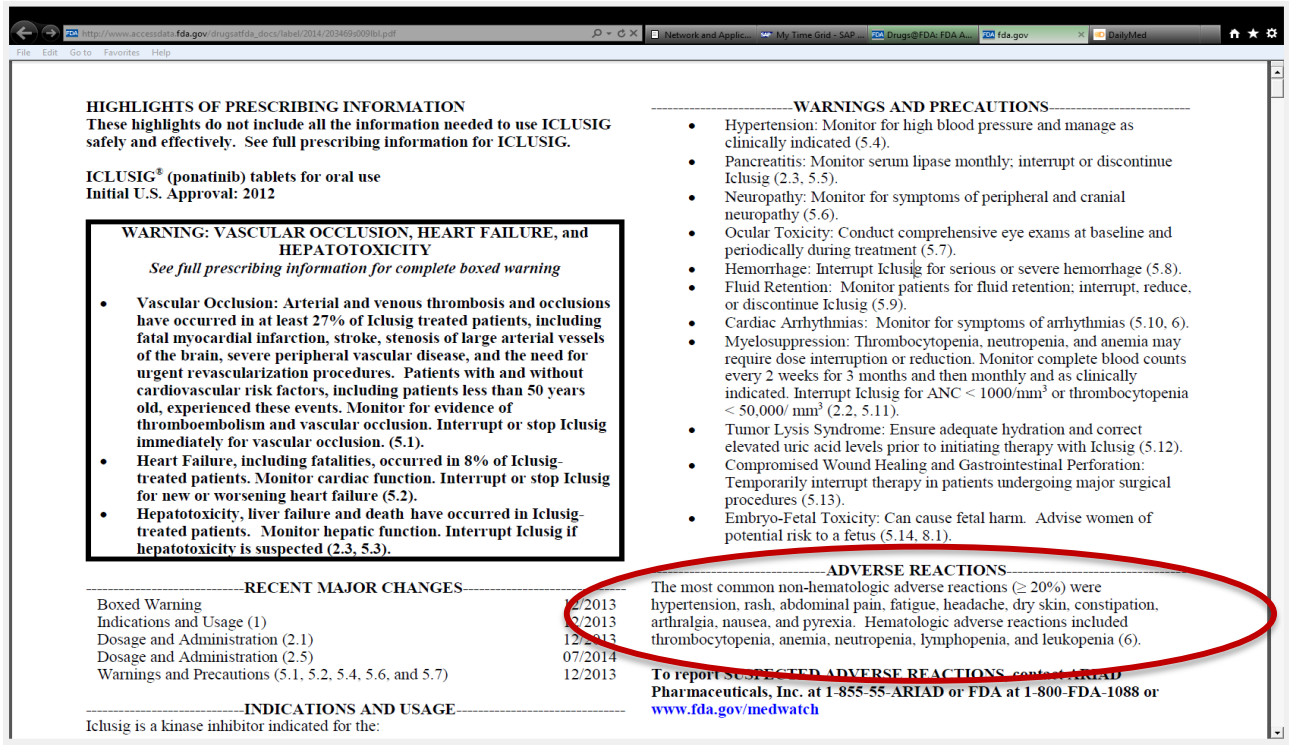
Extract Information from Related Products

- Start at the end – with a label
- Drugs for same indication,

  or
- Drugs of the same class



Extract Information from Related Products



HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ICLUSIG safely and effectively. See full prescribing information for ICLUSIG.

ICLUSIG® (ponatinib) tablets for oral use
Initial U.S. Approval: 2012

WARNING: VASCULAR OCCLUSION, HEART FAILURE, and HEPATOTOXICITY
See full prescribing information for complete boxed warning

- **Vascular Occlusion: Arterial and venous thrombosis and occlusions have occurred in at least 27% of Iclusig treated patients, including fatal myocardial infarction, stroke, stenosis of large arterial vessels of the brain, severe peripheral vascular disease, and the need for urgent revascularization procedures. Patients with and without cardiovascular risk factors, including patients less than 50 years old, experienced these events. Monitor for evidence of thromboembolism and vascular occlusion. Interrupt or stop Iclusig immediately for vascular occlusion. (5.1).**
- **Heart Failure, including fatalities, occurred in 8% of Iclusig-treated patients. Monitor cardiac function. Interrupt or stop Iclusig for new or worsening heart failure (5.2).**
- **Hepatotoxicity, liver failure and death have occurred in Iclusig-treated patients. Monitor hepatic function. Interrupt Iclusig if hepatotoxicity is suspected (2.3, 5.3).**

----------RECENT MAJOR CHANGES----------

Boxed Warning	12/2013
Indications and Usage (1)	12/2013
Dosage and Administration (2.1)	12/2013
Dosage and Administration (2.5)	07/2014
Warnings and Precautions (5.1, 5.2, 5.4, 5.6, and 5.7)	12/2013

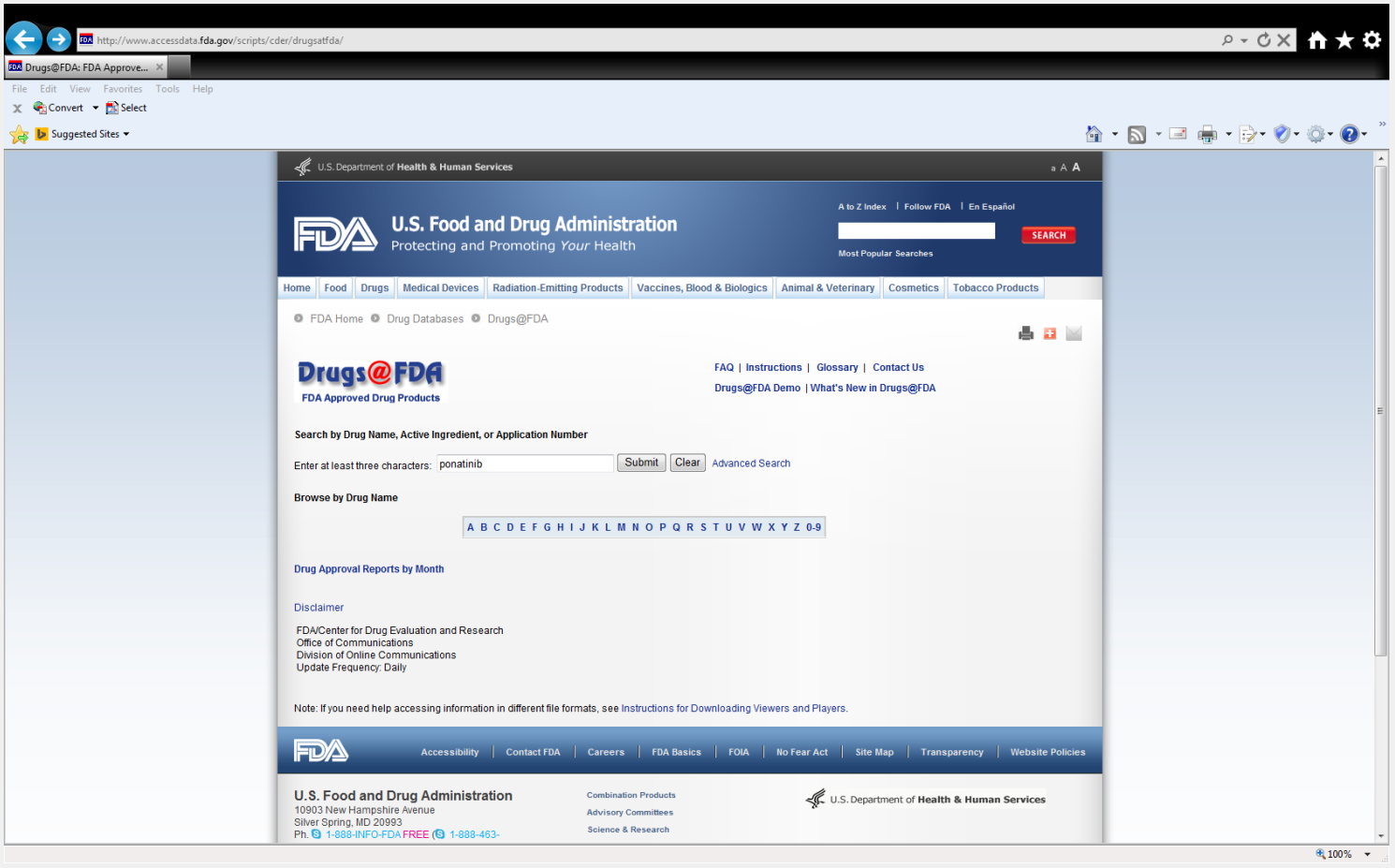
----------INDICATIONS AND USAGE----------
Iclusig is a kinase inhibitor indicated for the:

----------WARNINGS AND PRECAUTIONS----------

- Hypertension: Monitor for high blood pressure and manage as clinically indicated (5.4).
- Pancreatitis: Monitor serum lipase monthly; interrupt or discontinue Iclusig (2.3, 5.5).
- Neuropathy: Monitor for symptoms of peripheral and cranial neuropathy (5.6).
- Ocular Toxicity: Conduct comprehensive eye exams at baseline and periodically during treatment (5.7).
- Hemorrhage: Interrupt Iclusig for serious or severe hemorrhage (5.8).
- Fluid Retention: Monitor patients for fluid retention; interrupt, reduce, or discontinue Iclusig (5.9).
- Cardiac Arrhythmias: Monitor for symptoms of arrhythmias (5.10, 6).
- Myelosuppression: Thrombocytopenia, neutropenia, and anemia may require dose interruption or reduction. Monitor complete blood counts every 2 weeks for 3 months and then monthly and as clinically indicated. Interrupt Iclusig for ANC < 1000/mm^3 or thrombocytopenia < 50,000/ mm^3 (2.2, 5.11).
- Tumor Lysis Syndrome: Ensure adequate hydration and correct elevated uric acid levels prior to initiating therapy with Iclusig (5.12).
- Compromised Wound Healing and Gastrointestinal Perforation: Temporarily interrupt therapy in patients undergoing major surgical procedures (5.13).
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise women of potential risk to a fetus (5.14, 8.1).

----------ADVERSE REACTIONS----------
The most common non-hematologic adverse reactions (≥ 20%) were hypertension, rash, abdominal pain, fatigue, headache, dry skin, constipation, arthralgia, nausea, and pyrexia. Hematologic adverse reactions included thrombocytopenia, anemia, neutropenia, lymphopenia, and leukopenia (6).

To report SUSPECTED ADVERSE REACTIONS, contact ARIAD Pharmaceuticals, Inc. at 1-855-55-ARIAD or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch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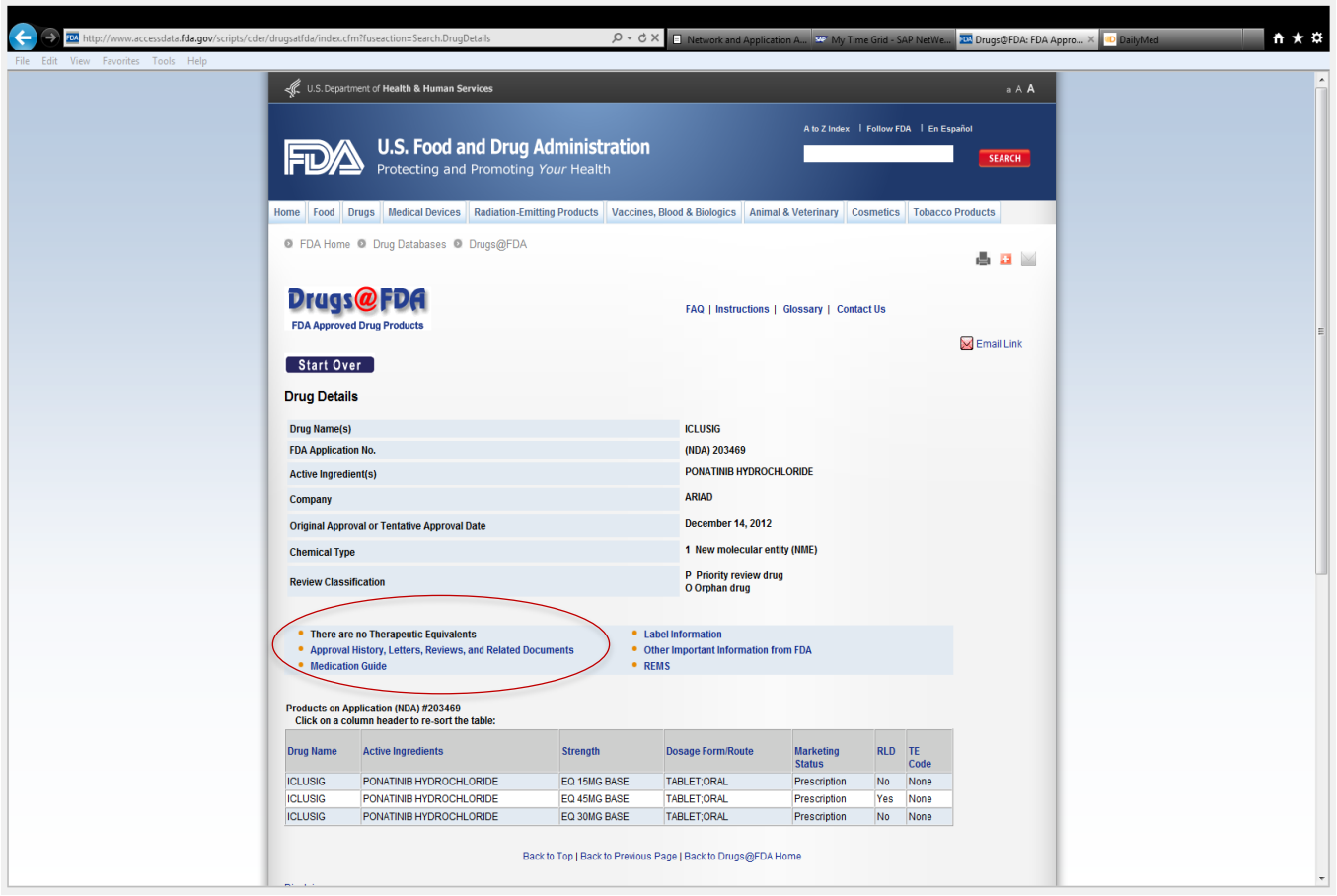

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Drug Details

Drug Name(s)	ICLUSIG
FDA Application No.	(NDA) 203469
Active Ingredient(s)	PONATINIB HYDROCHLORIDE
Company	ARIAD
Original Approval or Tentative Approval Date	December 14, 2012
Chemical Type	1 New molecular entity (NME)
Review Classification	P Priority review drug O Orphan drug

- There are no Therapeutic Equivalents
- Approval History, Letters, Reviews, and Related Documents
- Medication Guide
- Label Information
- Other Important Information from FDA
- REMS

Products on Application (NDA) #203469
Click on a column header to re-sort the table:

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	RLD	TE Code
ICLUSIG	PONATINIB HYDROCHLORIDE	EQ 15MG BASE	TABLET;ORAL	Prescription	No	None
ICLUSIG	PONATINIB HYDROCHLORIDE	EQ 45MG BASE	TABLET;ORAL	Prescription	Yes	None
ICLUSIG	PONATINIB HYDROCHLORIDE	EQ 30MG BASE	TABLET;ORAL	Prescription	No	None

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Advisory Committee Materials

- Advisory Committee Briefing Materials: Available for Public Release

- **Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee Meeting Announcement**

- **December 12, 2017**

- Premarket Approval Application (PMA) for the Barricaid Anular Closure Device by Intrinsic Therapeutics

Guidance Documents

- **Respiratory Syncytial Virus Infection: Developing Antiviral Drugs for Prophylaxis and Treatment**
- **Guidance for Industry**
- ***DRAFT GUIDANCE***
- **U.S. Department of Health and Human Services**
- **Food and Drug Administration**
- **Center for Drug Evaluation and Research (CDER)**
- **October 2017 Clinical/Antimicrobial**

Key Aspects of Successful Regulatory Strategies

- Identify the potential patient population(s)
- Understand how the product would be used clinically – how will it fit in with current standards of care?
- Know what went before – what measures of efficacy and safety are accepted by the clinical community?
- Identifies competitor compounds in development or already on the market?
- Clarifies studies required to support safety prior to initiating “first in man” studies
- Defines potential label claims that should be considered in developing a clinical plan
- Identify regulatory approval options that could speed entry to the clinic?
- Determine questions that should be posed to the FDA before getting too far down the road?

Probability of Success

- The probability of success (POS) of a development strategy is critical for clinical researchers and biopharma investors to evaluate when making scientific and economic decisions.

- Prudent resource allocation relies on the accurate and timely assessment of risk. Without up-to-date estimates of the POS, however, investors may misjudge the risk and value of drug development, leading to lost opportunities for both investors and patients.

- One of the biggest challenges in estimating the success rate of clinical trials and ultimately the right choice of a clinical indication is access to accurate information on trial characteristics, patient characteristics, and outcomes.

Thank You!

Open for Questions

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Feedback Survey

A link to the feedback survey has been sent to the email address you used to register.

Please get out your device, find that email, and spend a few moments completing that survey before you leave today.

Tip: If on a mobile device, shift view to landscape view (sideways) for better user experience.