A Pathway for Patents

Understanding pharmaceutical patents and their intersection with the FDA

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Overview

- What is a Patent?
- Details Unique to a Drug Patent
- Getting a Patent: Start to Finish
- Patents and the FDA
  - Biosimilars Price Competition and Innovation Act (BPCIA) not included.
- Questions

What is a Patent?

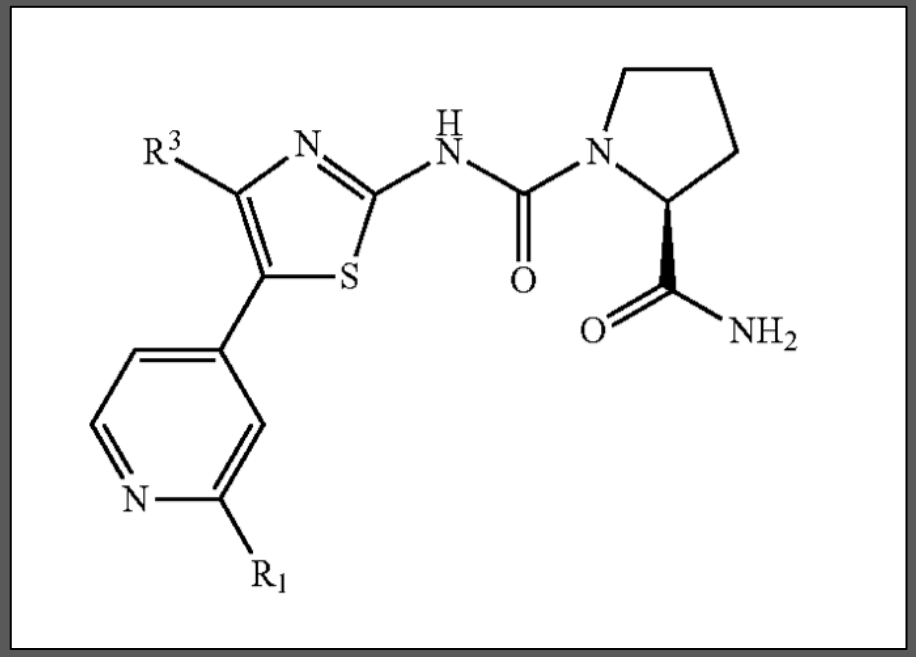
- A limited monopoly to an invention
  - Exclude others to *make, use, sell, or import* the invention
  - For the patent's "term"
- Government granted exclusion in exchange for disclosure
  - "To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries" - *US Constitution,* Article I, Section 8, Clause 8
  - Contrast with Trade Secrets

What is a Patent?

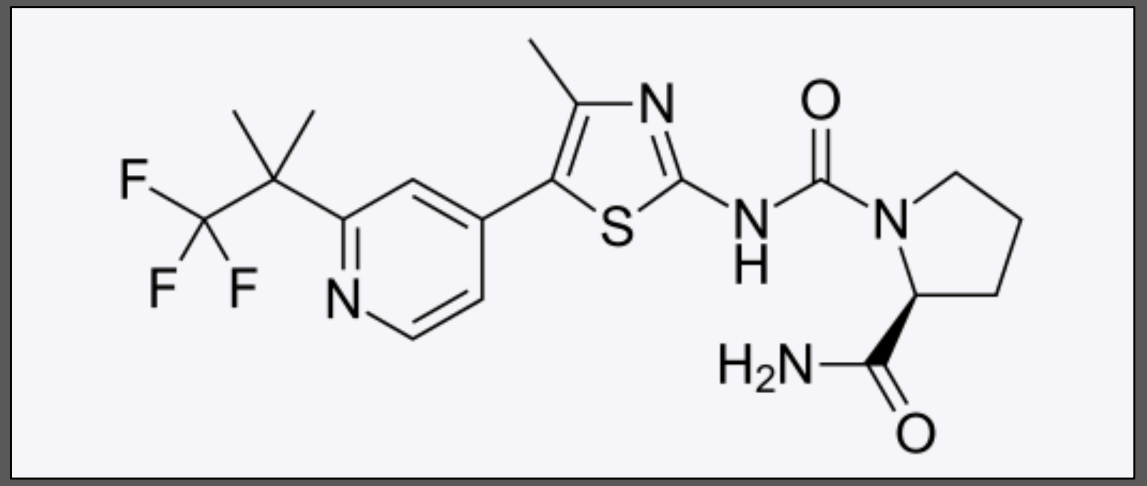
- Specification
  - Provide the workings of your technology
  - Enablement
  - No "undue experimentation”
  - "One of skill in the art"
- Claims
  - Legal definition of the invention
  - Provides the metes and bounds of your right to exclude
  - "Infringing" activity must "read on" your claims in order to sue

Drug Patents – Small Molecule

- Markush structure



Alpelisib – US Pat. No. 8,476,268



Alpelisib

Small Molecule Drugs

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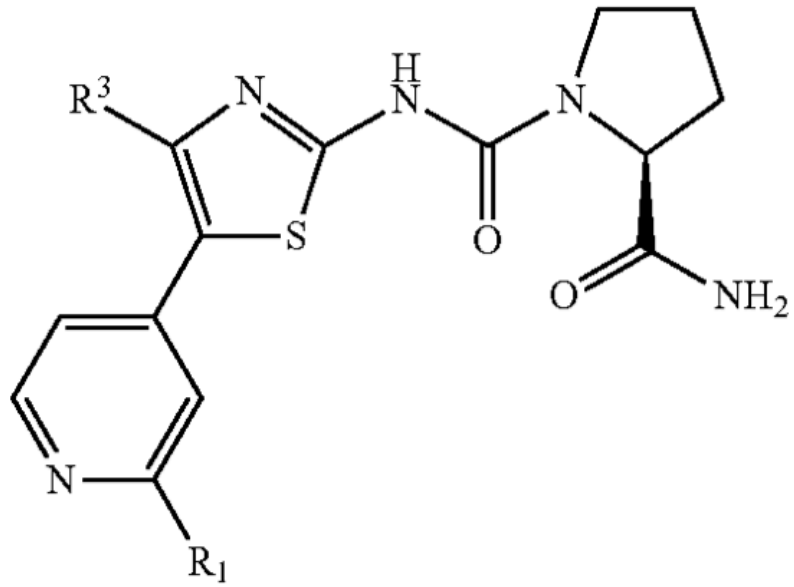

R^3 is selected from: hydrogen; fluoro; chloro; and optionally substituted methyl; wherein said substituents are independently selected from one to three of the following moieties: deuterium, fluoro, chloro and dimethylamino.

R^1 represents one of the following substituents: (1) substituted, C_1-C_7-alkyl, wherein said substituents are independently selected from one to nine of the following moieties: deuterium and fluoro, or one to two of the following moieties: C_3-C_5-cycloalkyl; (2) optionally substituted C_3-C_5-cycloalkyl wherein said substituents are independently selected from one to four of the following moieties: deuterium, methyl, fluoro, cyano and aminocarbonyl; (3) optionally substituted phenyl wherein said substituents are independently selected from one to two of the following moieties: deuterium, halo, cyano, C_1-C_7-alkyl, C_1-C_7-alkylamino, di(C_1-C_7-alkyl)amino, C_1-C_7-alkylaminocarbonyl, di(C_1-C_7-alkyl)aminocarbonyl and C_1-C_7-alkoxy; (4) optionally mono- or di-substituted amine; wherein said substituents are independently selected from the following moieties: deuterium; C_1-C_7-alkyl which is unsubstituted or substituted by one or more substituents selected from deuterium, fluoro, chloro and hydroxy; phenylsulfonyl which is unsubstituted or substituted by one or more groups selected from C_1-C_7-alkyl, C_1-C_7-alkoxy and di(C_1-C_7-alkyl)amino-C_1-C_7-alkoxy); (5) substituted sulfonyl; wherein said substituent is selected from the following moieties: C_1-C_7-alkyl which is unsubstituted or substituted by one or more substituents selected from deuterium and fluoro; and pyrrolidino which is unsubstituted or substituted by one or more substituents selected from deuterium, hydroxy and oxo; (6) fluoro and chloro; and

Drug Patents – Small Molecule

- Markush structure
  - For enablement: a species discloses its genus, a genus does not disclose all species*
- Be wary of hindsight

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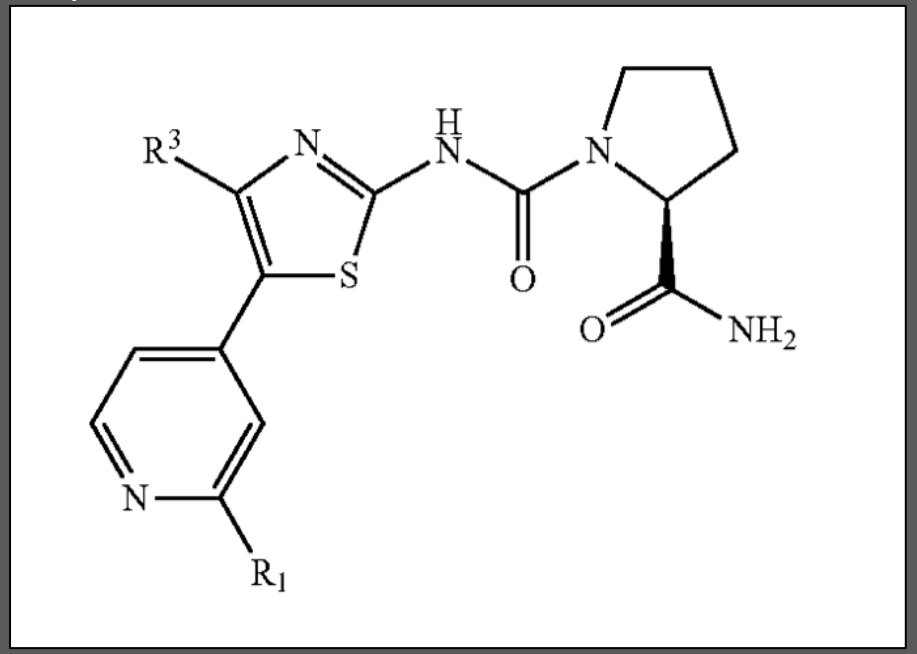

Drug Patents – Small Molecule

- Markush structure
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- Be wary of hindsight
- Salts, esters, prodrugs, isotopomers
- Chirality
  - Possible enablement issues

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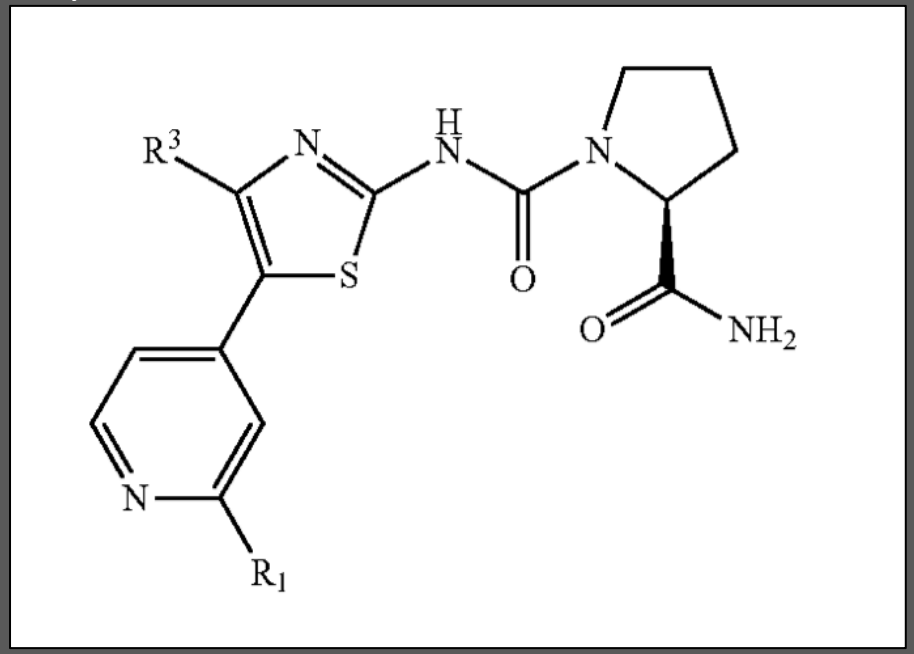


Drug Patents - Biologics

- Developing field
  - Claiming strategies are changing
- Isolated products of nature exclusion
- Homology limitations

Bevacizumab* - US Pat. No. 6,407,213

79. A humanized variant of a non-human parent antibody which binds an antigen, wherein the humanized variant comprises Complementarity Determining Region (CDR) amino acid residues of the non-human parent antibody incorporated into a human antibody variable domain, and further comprises Framework Region (FR) substitutions at heavy chain positions 71H, 73H, 78H and 93H, utilizing the numbering system set forth in Kabat.

*Claim from a patent cited in Genetech's list against Amgen during ongoing "patent dance" litigation
Amgen v. Genentech, C.D. Cal., Case No. 17-cv-7349

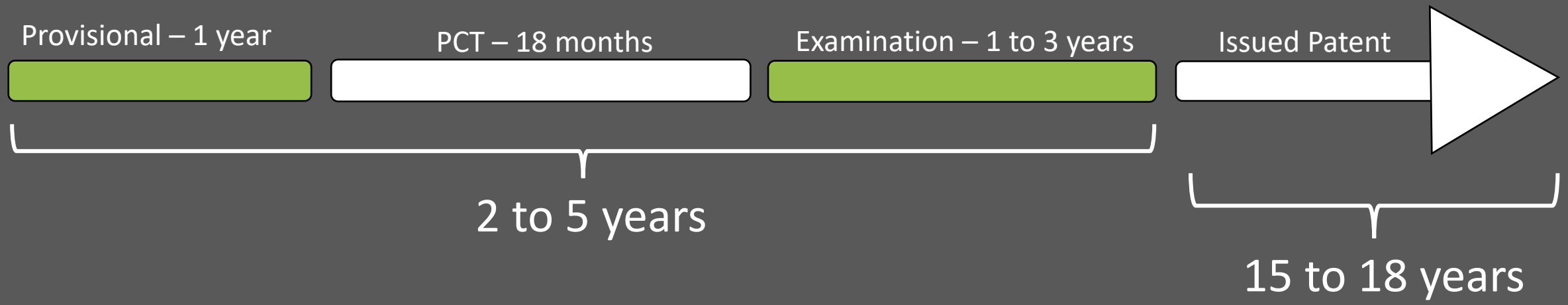
Drug Patents – Other subject matter

- Formulations
- Methods of manufacture
  - Necessary for enablement
  - Benchtop vs. Scale-up
- Methods of treatment
  - Disease indications
  - Drug repurposing

Alpelisib – US Pat. No. 8,476,268

4. A method of treatment of a proliferative disease, comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound of claim **3** in free form or in pharmaceutically acceptable salt form, wherein the proliferative disease is selected from the group consisting of melanoma, colorectal adenoma and cancers of the breast, and pancreas.

Lifetime of a patent



Provisional Applications

- Stake your claim!
  - Preserve your filing date
  - Keep out ”prior art” – including your own
- Up to one year to "convert"
- Minimal requirements / no examination
  - Enablement still required
- Limited publication

Patent Cooperation Treaty (PCT)

- One application -> many countries
- Extended timelines to select which nations/jurisdictions you'd like to pursue
  - About 18 months
- Filing fees and translation costs
- Possible to skip this step

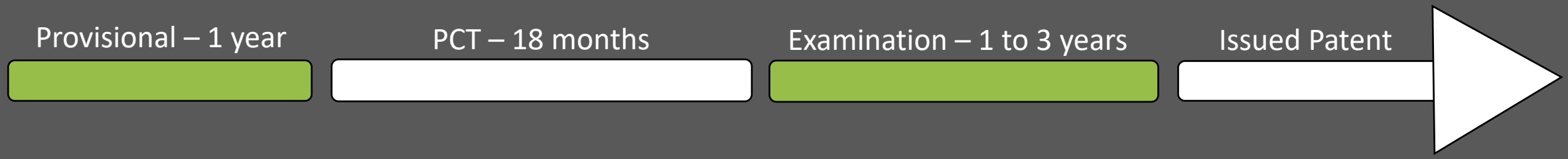
National Examination (Prosecution)

- Review of your application by patent examiners
  - "Office Actions”
  - About 1-3+ years
- Analysis for utility, novelty, non-obviousness, enablement
- Fear no rejections

Issuances

- Issued patents are the enforceable documents
  - "Patent pending" gives notice to competitors
- 20 years from filing
  - Maintenance fees
- You must enforce your own IP rights.
  - Injunction to stop the infringing activity.
  - Damages from the infringing activity (up to 6 years in back damages)

FDA Regulation and Patents



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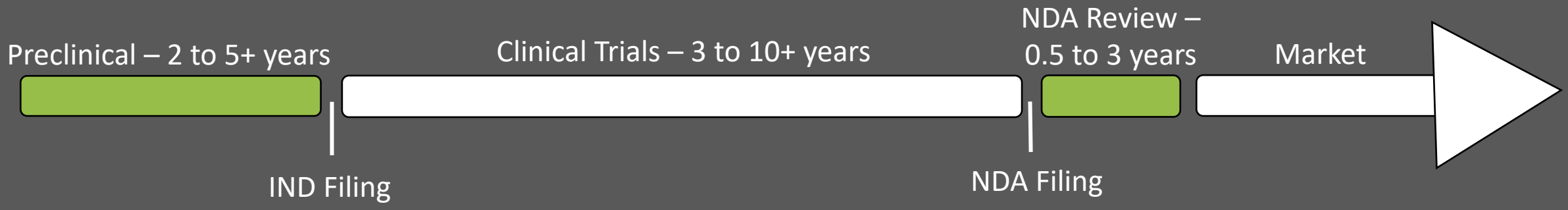

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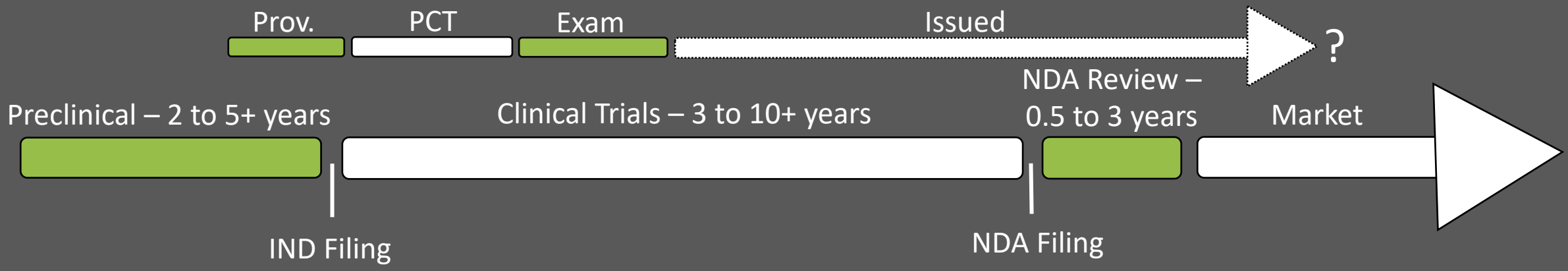

FDA Regulation and Patents

- "Wasted"/"Bonus" patent term
- "Experimental use" infringement
- Hatch-Waxman Act (1984) provision
  - Generics & Safe Harbor
  - Data and Market Exclusivities
  - Patent Term Extension
  - The Orange Book

Generics, ANDAs, and Paragraph IV

- Abbreviated New Drug Applications (ANDAs)
- Safe Harbor Provision
- Paragraph IV
  - Early ANDA filing stating non-infringement or invalidity
  - 180-day market exclusivity on successful challenge

FDA – Data Exclusivity

- New chemical entities only
  - "Active moiety" - regardless of salts/prodrugs/formulations
- 5 years prohibition on competing application filings (usually ANDAs)
  - WARNING: 4 years and a day - Paragraph IV
- No patents required

FDA – Market Exclusivity

- New formulations/dosages/indications
  - "Old drug in a new way"
- 3-year prohibition on approval of competing applications
  - No barrier to Paragraph IV
  - Watch for Section VIII carve-outs
- No patents required

Patent Term Extension

- Patent Term Extension (PTE)
  - Effectively only for NCEs

    PTE = NDA review time + ½ time between IND and NDA filing
  - 5 year maximum - Lifetime remaining cannot exceed 14 years
  - Only one patent can be extended - Extension only covers relevant claims

The Orange Book

- Listing of relevant patents in the Orange Book is required
  - Composition, formulation, or use patents only
  - Improper listing liable under perjury
  - Small molecule drugs only (BPCIA)

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