CRITICAL PATH INSTITUTE 20 YEARS OF IMPACT

Therapeutic Development Learning Community: Intellectual Property in Drug Discovery and Development Projects

Maaike Everts, Mary O'Reilly, Joanna Yang Yowler & Mark Drew (USPTO #72,496)

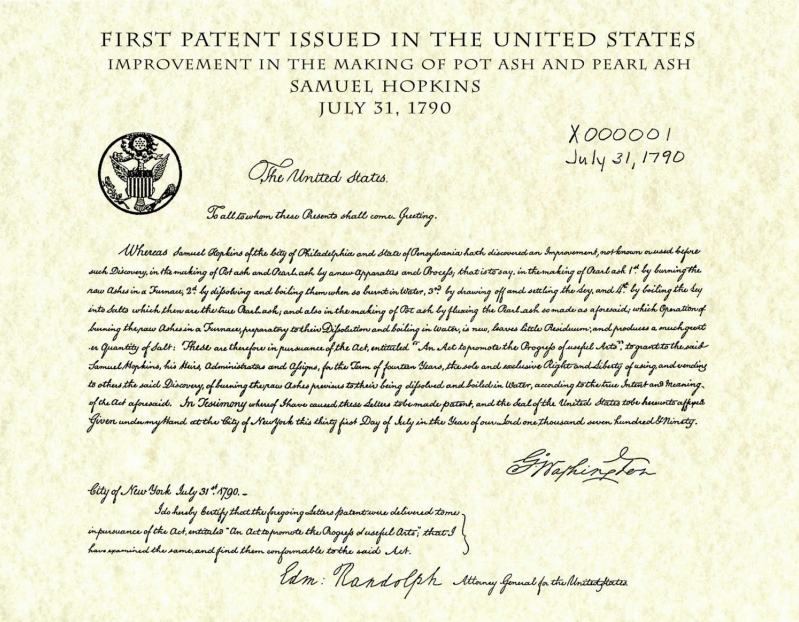
A Brief History of Patent Law

1790: 1st US Patent Act entitled "*An act to promote the progress of useful arts*"

1850: Introduction of the concept that an invention must be non-obvious as well as new and useful

1978: Patent Cooperation Treaty put into effect; allows single worldwide filing

1980: Bayh-Dole Act – Universities retain title to results of Federally funded research



FIRST PATENT ISSUED IN THE UNITED STATES

IMPROVEMENT IN THE MAKING OF POT ASH AND PEARL ASH

SAMUEL HOPKINS

JULY 31, 1790

X0000001
July 31, 1790

The United States.

To all to whom these Presents shall come, Greeting.

Whereas Samuel Hopkins of the city of Philadelphia and State of Pensylvania hath discovered an Improvement, not known or used before such Discovery, in the making of Pot ash and Pearl ash, by a new Apparatus and Process, that is to say, in the making of Pearl ash 1st by burning the raw Ashes in a Furnace, 2d by dissolving and boiling them when so burnt in Water, 3d by drawing off and settling the ley, and 4th by boiling the ley into salts which then are the true Pearl ash; and also in the making of Pot ash, by flowing the Pearl ash so made as aforesaid, which Operation of burning the raw Ashes in a Furnace, preparatory to their Dissolution and boiling in Water, is new, leaves little Caruidum, and produces a much greater Quantity of salt: These are therefore in pursuance of the Act, entitled "An Act to promote the Progress of useful Arts", to grant to the said Samuel Hopkins, his Heirs, Administrators and Assigns, for the Term of fourteen Years, the sole and exclusive Right and Liberty of using and vending to others the said Discovery of burning the raw Ashes previous to their being dissolved and boiled in Water, according to the true Intent and Meaning of the Act aforesaid. In Testimony whereof I have caused these Letters to be made patent, and the Seal of the United States to be hereunto affixed. Given under my Hand, at the City of New York this thirty first Day of July in the Year of our Lord one thousand seven hundred & Ninety.

G. Washington

City of New York July 31st 1790.–

I do hereby certify that the foregoing Letters Patent were delivered to me in pursuance of the Act, entitled "An Act to promote the Progress of useful Arts", that I have examined the same, and find them conformable to the said Act.

Edm: Randolph Attorney General for the United States

1st US patent issued July 31st, 1790, to Samuel Hopkins for the '*improvement of making pot ash and pearl ash*' which revolutionized the pot ash industry and allowed urchins living in Thomas Hardy novels to have ideas above their stations.

What is Intellectual Property

- Protection of corporate assets (IP = Idea Protection)

35 U.S. Code § 101 – Patentable inventions :

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

- A legal protection which gives an inventor the right to exclude others from performing certain activity in the country of issuance
- Sanctioned monopoly for a set number of years in exchange for disclosure to the public
- Originates from U. S. Constitution – "To Promote the Progress of Science and useful Arts…"

What TRxA Requires

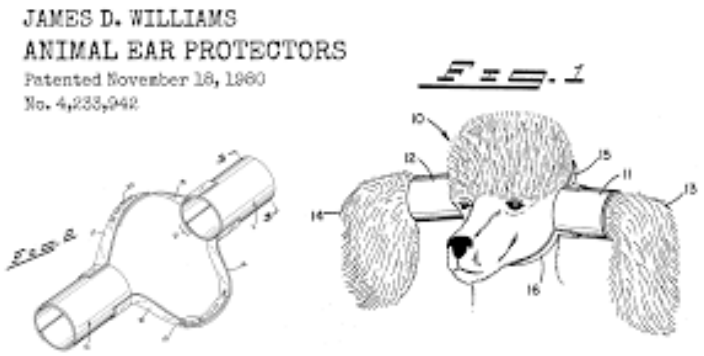
- **Novel** chemical matter (small molecule, biologic etc.) that shows a measurable response in a translational assay and/or an animal model that would addresses an unmet need.

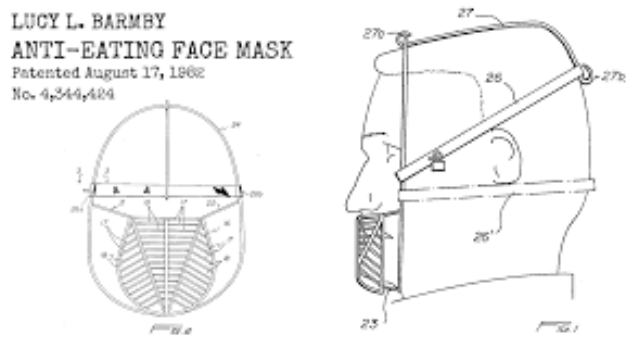
- Also needs to have an articulable strategy for regulatory approval
  - A defined patient population, a clinical biomarker,…

- **Also needs to be attractive to biotech, pharma or venture capital**
  - **$$$ is going to be required to advance into and through the clinic**
  - **A return on investment (ROI) is a prerequisite requirement**
  - **An ROI requires a protectable asset**

Not All Patents are Created Equally

- You can obtain a patent on lots of weird inventions, but it might not be worth time and money:

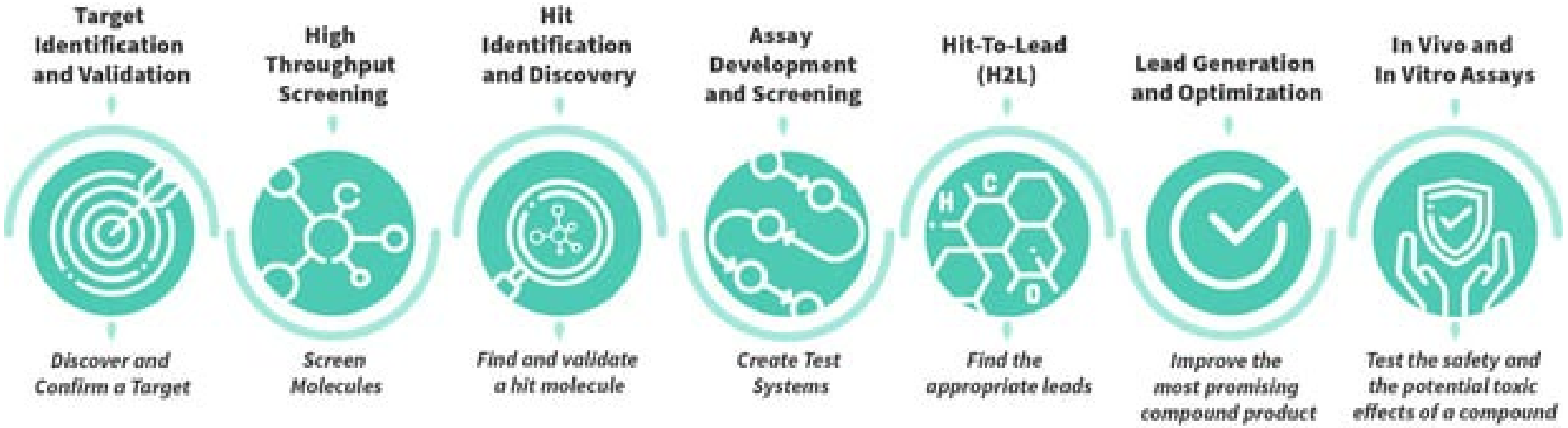




- Questions to consider:
  - Is there a market for the product?
  - How easy is it for competitors to make something close and functional?
  - Would owing IP on the technology make a start-up attractive to investors?
  - Will this open licensing opportunities?

Life-Cycle of a Drug Discovery Project

- The science underpinning a drug discovery project may or may not be patent eligible

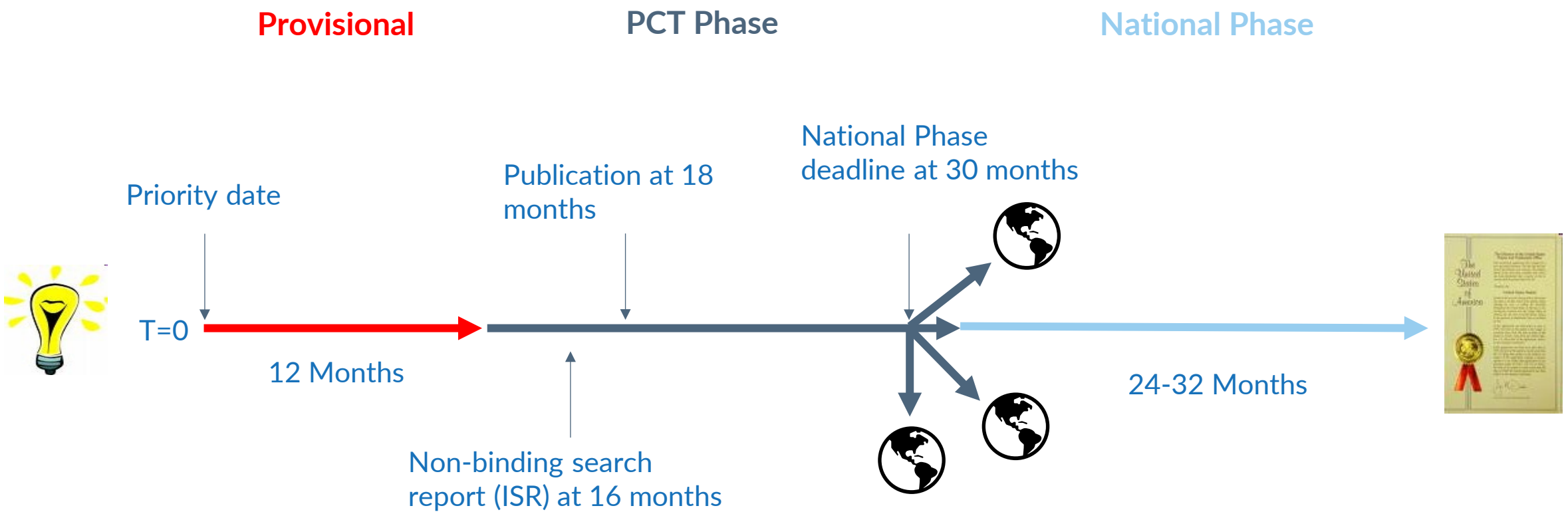


- The discovery of a druggable **target** (found in nature) would not be patent eligible
  - But it is a foundational discovery that enables the scientific community → open science?
- A biochemical assay/transgenic animal model to discover modulators of the target may be patent eligible
  - But is difficult to enforce → open science?
- The chemical compounds discovered are likely patent eligible

General Steps for Obtaining a Patent

1. Disclose your invention and work with a patent lawyer/agent to write a patent
2. File a provisional patent application
3. Within a year, file a PCT application
4. Within 30 months convert to non-provisional application(s) in desired countries
5. Patent prosecution
6. Allowance and issue

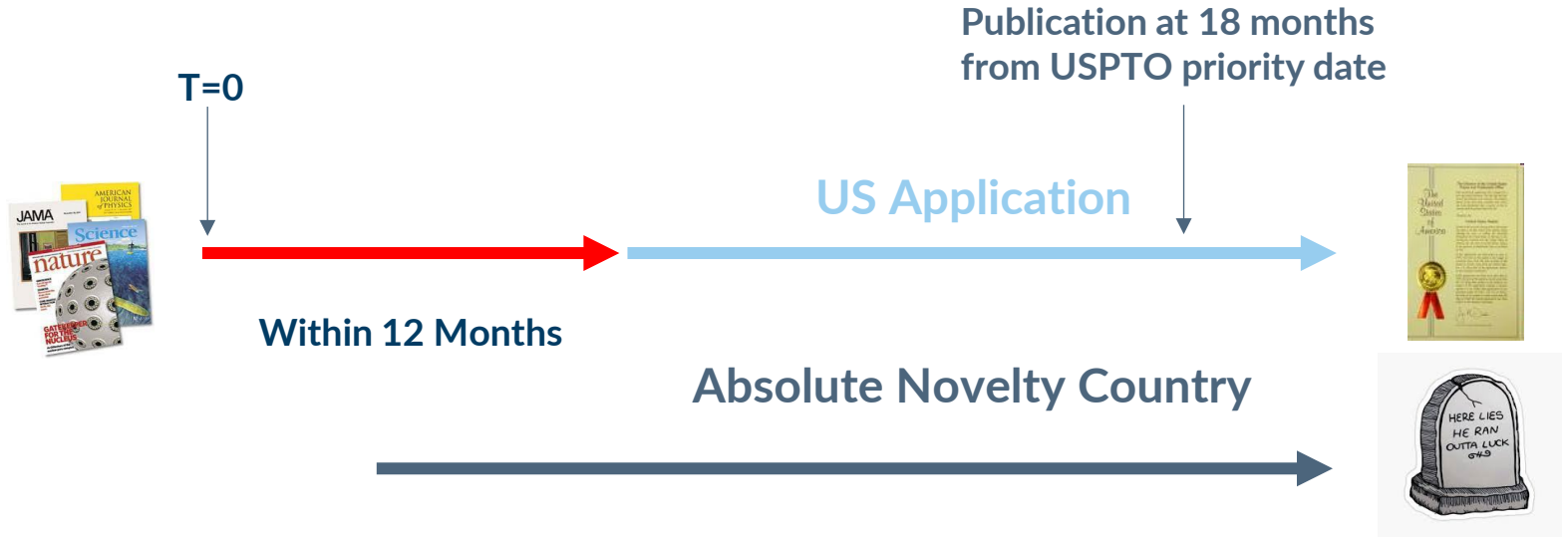
Timeline to Obtain Patent Protection



- A provisional application does not publish, is not examined, does not require claims or a format
  - Sets a priority date
- A priority date sets the bar for all that is 'prior art'

Why a Priority Date is Important

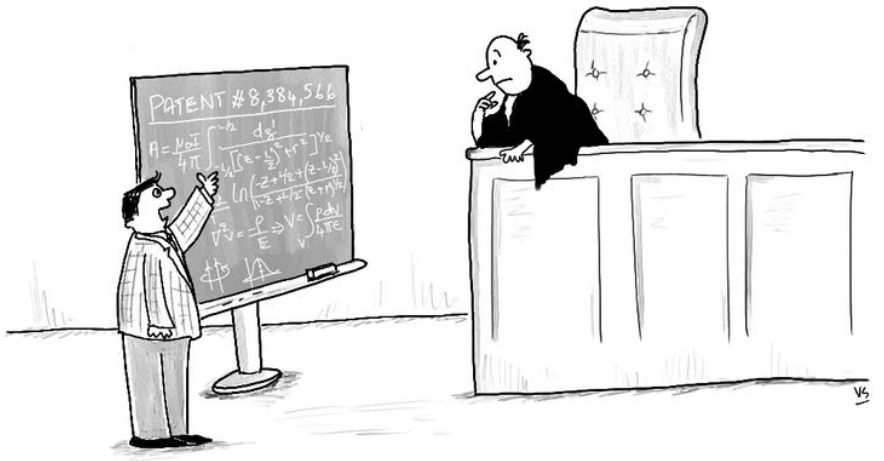
- The US allows a 1-year grace period from disclosure to file an application (inc. Provisional)
  - Publicly disclose and then within 1 year file a patent application
- Many countries require absolute novelty (Germany, UK, France, Italy, China,…)
  - An application must be filed before activities that would constitute prior art



- While it is true that some grace-period does remain in the US, you should not rely on the grace-period. At best, the grace-period should be thought of as a possible way to **address the mistake** of not having filed first.

Important Sections of US Patent Law

- 35 U.S.C. § **101**: Concerns **patent eligible** subject matter
- 35 U.S.C. § **102**: **Novelty**. Anticipated if comparison of the claimed invention with a prior art reference reveals that each and every element in the claim under attack is shown or described
- 35 U.S.C. § **103**: **Obviousness.** A patentable invention must not have been obvious to a "*person having ordinary skill in the art*" (PHOSITA) in view of the appropriate prior art.
- 35 U.S.C. § **112**(b): Written description/**enablement**. A patent application will only be allowed to issue as a patent if the written disclosure is enabling.



"So you see your honor, it's obvious."

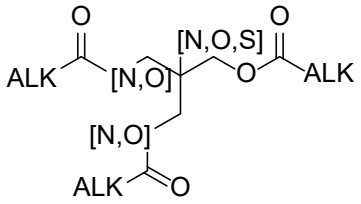
How C-Path Assesses Projects

- C-Path does not require our applicants to have acquired a patent, however the project must be 'patent eligible'

- Patent eligible is defined as no 102 bars, i.e. the structure is not disclosed
  - Projects with method of use patents are less attractive to reviewers

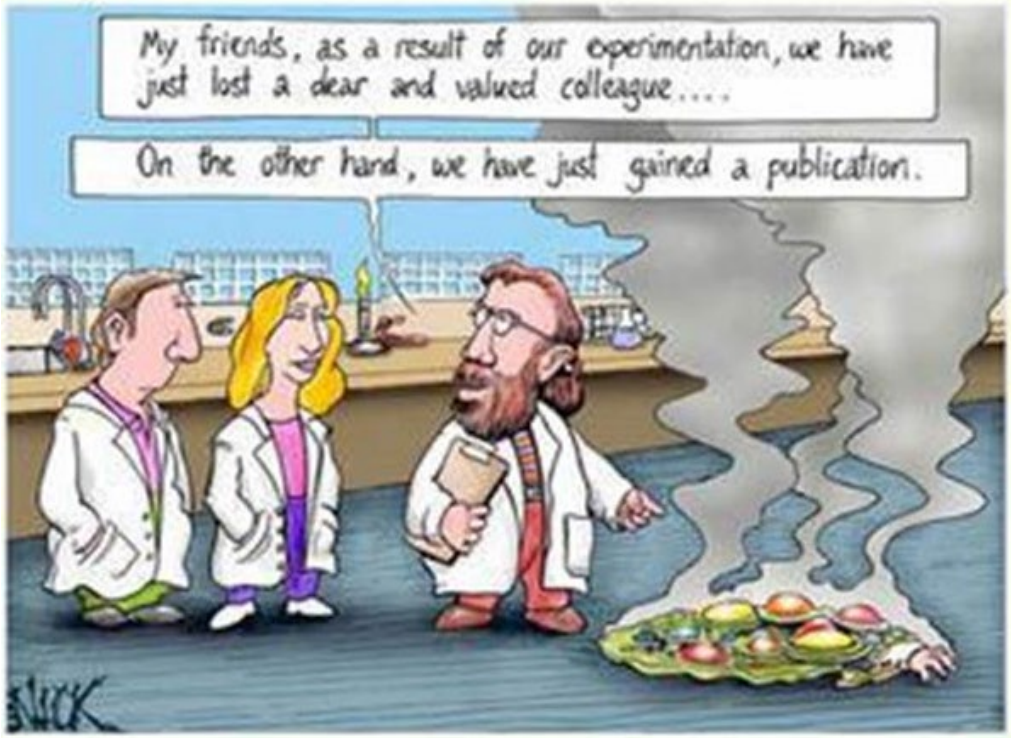
- We carry out due-diligence searches on a Markush structure of their candidate
  - If an ISR is available, we look at flagged documents
  - Structure disclosure of lead candidate or SEQ listing → SciFinder, REAXYS, PatSnap Chem

- **Example: Orally available compound suppresses glucagon hypersecretion**
  - Not progressed due to candidate not being patent eligible
  - Surprise to the PI. They and their TTO were preparing their COM patent application:



- **Chemische Berichte**, **1897**, vol. 30, p. 2058

Academic Publish or Perish Culture



- In academics there is an emphasis on “first to publish”
  - Required for students to show accomplishments to advance their careers.
  - Academics are under pressure to increase their publication count to establish their expertise in their field.
  - Researchers with limited exposure to the worth of a patent may be unaware of the significance of keeping their key research findings confidential.

- **The need to publish can be contrary to the requirement of protecting your asset**
- **Publication should not jeopardize IP rights**

Academic Publish or Perish Culture

1. Talk to the institution's Technology Transfer Office and Intellectual Property (IP) offices to develop strategies for ensuring patent protection.
    a. TTOs have metrics that may not be in the PIs best interest.
2. University Leadership should be encouraged to value IP as a metric
3. File a patent before presenting or publishing the work in the public domain.
4. Generate data concurrently on a 'tool molecule' and the 'lead series', e.g. a tool could be a known drug or a candidate with a fatal flaw that allows POC data to be generated and disclosed.
5. Utilize scientific staff rather than students.
6. Use codes to describe your data, elements, or any principal components, do not disclose structures.
7. Manage the 'patent clock'.

Case Example: The Need to Publish

TRxA Funded a successful GBM Project in 2023:

- Co-I had an invitation to publish in a prestigious journal
- Animal efficacy data was generated by a doctoral student within the Co-I's lab
- The journal requires disclosure of structure
  - POC efficacy had been generated on an 'early' candidate:
    - However, the 'early' candidate is structurally similar to the 'development' candidate (95% Tanimoto coefficient)
    - Disclosure could alert competitors to the development candidate
    - Publication may generate prior art to any subsequent filings

- Work has been accepted for publication in a high-impact journal without disclosure of the structure. Only the compound reference number is disclosed (DYR-726)

Common Questions on Process Flow

Provisional

1. A provisional application does not have a format and doesn't require claims
   - Usually written as a utility application for easy conversion
2. Not examined but must enable and fully disclose.
   - May lose priority for new material added at conversion
3. Does not start the clock on patent term

PCT

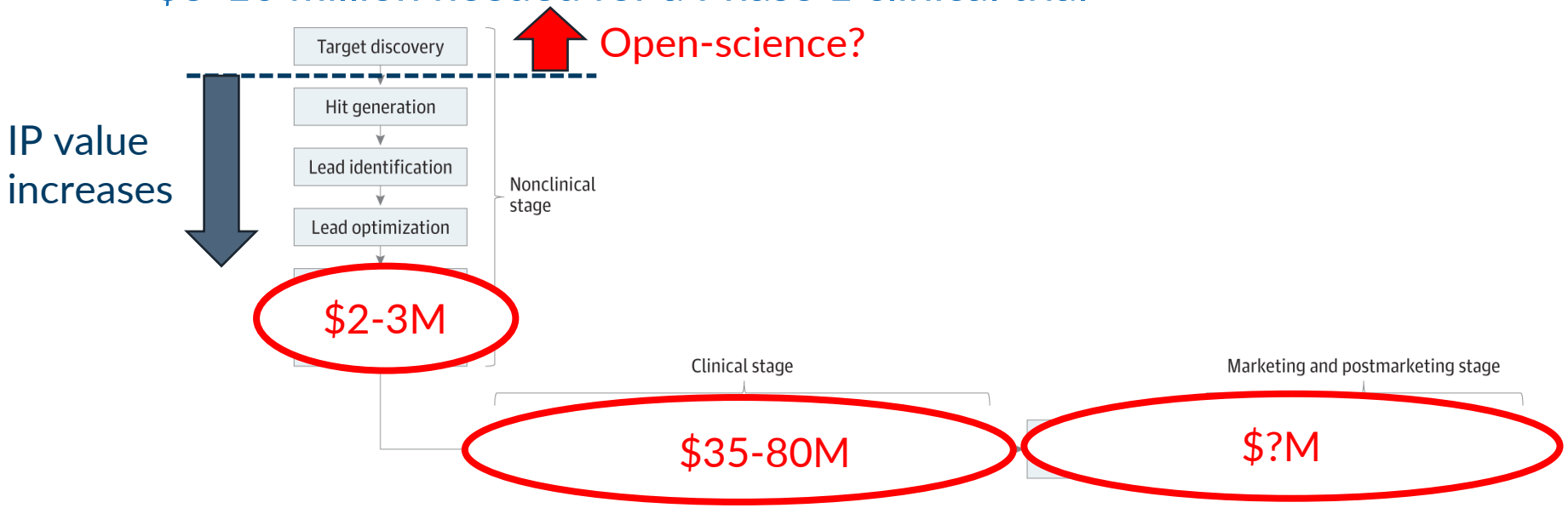
1. Does not convey any rights, this is not a 'worldwide patent'
2. Chose which countries you'll file in (leave blank and default to all 158 PCT members)
3. At around 30 months (Luxembourg and Tanzania are 20/21 months, some are 31 months) convert into chosen countries.
4. Starts the clock on the 20-year US patent term
5. 4 PCT sites worldwide, file in the designated country of invention (likely USPTO)

National Phase

1. Assigned to an Art Unit at the USPTO
2. A single examiner will be responsible for the application
3. Rejections are common and countered by arguments or amendments
4. Expensive and lengthy process depending on Art Unit (Allowance varies from 7.7 - 98.3%)

Why File a Patent in Life Science

- The average cost of pre-clinical and clinical studies are substantial:
  - $2-3 million for IND-enabling studies
  - $5-10 million needed for a Phase 1 clinical trial



- $7-20 million Phase 2; $11-50 million Phase 3; $12-33 million post-approval
- Manufacturing, formulation, labelling, shipping…..

From: **Costs of Drug Development and Research and Development Intensity in the US, 2000-2018,** JAMA Netw Open. 2024;7(6):e2415445. doi:10.1001/jamanetworkopen.2024.15445

The Layers of Patent Protection

- In an ideal scenario a drug product would have multiple layers of protection:
  - Drug Substance (the API)
    - Salt form
    - Polymorph
    - Formulation (drug product)
    - Method of Synthesis
  - Method of use for treatment of an indication

- Once a product is in the clinic it is good to have either protected or disclosed all of the above (if an advantageous salt or polymorph is available) so a third party can not file and force you to acquire a license
- Multiple layers of protection guards against invalidation of a single patent
  - Generics companies for example can realize high profits via this strategy

Protecting Repurposed Drugs

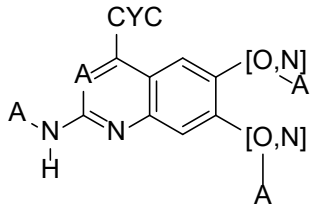
- You can have a scenario in which one entity owns the ‘composition of matter’, and another owns the ‘method of use’
  - In this case, either party would need to license the rights to the others’ patent to not infringe the others’ patent.

- You **can** get method of use claims on a known off-patent drug
  - You would not be infringing any valid patent
  - However, a party challenging the patent only needs to show that it would have been obvious to include this particular drug among numerous other drugs being screened in the treatment of a disease
- Enforcing your patent is challenging
  - The off-label prescriber would be the infringer

IP in Sponsored Projects: Case Example

Modulator For The Treatment of a Rare Disease:

- Development candidate (MS-1):



Development Candidate MS-1

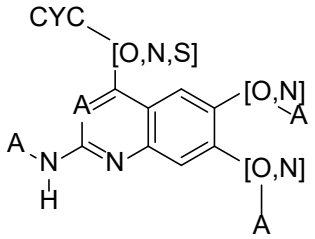
Prior Art Found on MS-1:

- Composition of matter is owned by another: **April 2016 priority date (granted)**
- Claimed in method of use application for the same rare disease indication: **March 2017 priority date (abandoned)**
- PI has not filed an application, i.e. they have no priority date
- Continuing developing MS-1 would be infringement of the granted composition of matter patent
- A method of use for the treatment of the indication application is barred by the publication of the others' abandoned application

IP in Sponsored Projects: Case Example

Modulator For The Treatment of a Rare Disease:

- Back-up candidate (MS-2):



Back-up Candidate
MS-2

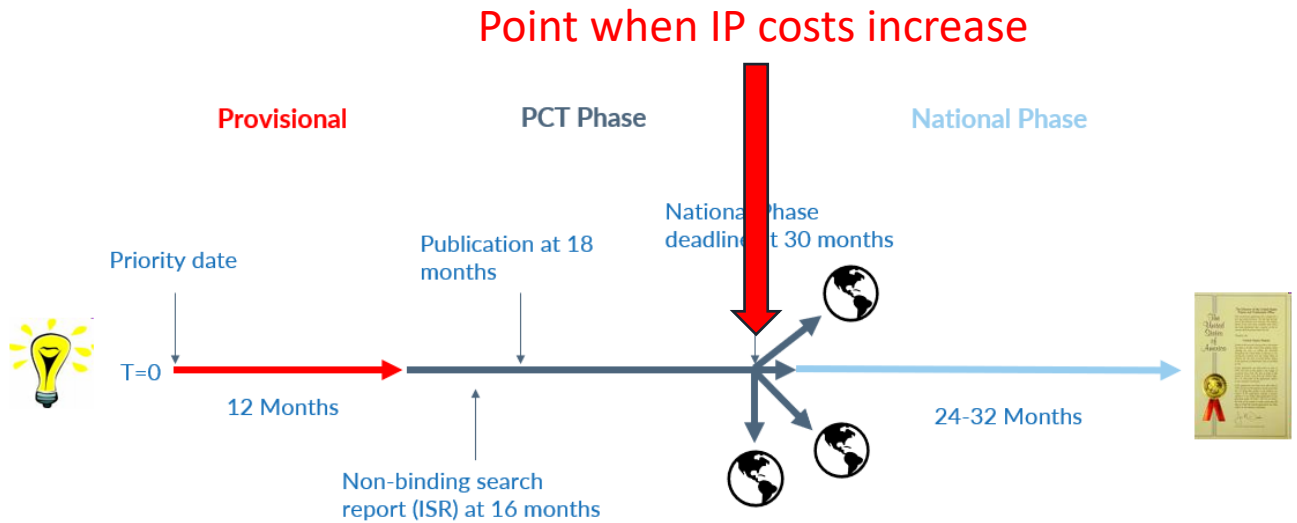
Prior Art Found on MS-2:

- A close structure was disclosed in non-patent literature by the PIs in 2013 (>1 year)
  - This is a bar to filing a composition of matter application
- A method of treatment of the indication patent is granted: **May 2016 priority date**
  - The structure of MS-2 is covered within the granted claims
- The PIs submitted a new application with claims to method of treatment and composition of matter has been filed: **July 2023 priority date**
  - No FTO concern, but obtaining a patent will require arguing around their own 2016 granted patent

The Patent Clock

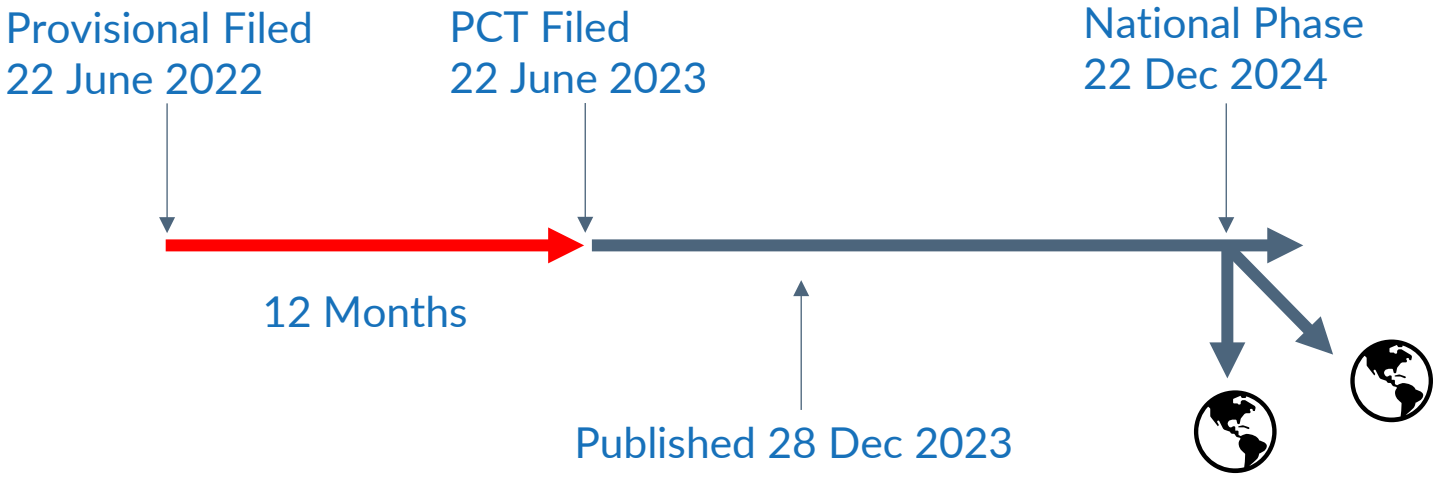
- The term of a US patent is 20 years from the effective filing date (not provisional).
  - You can get time back (usually days-weeks) for delays caused by the patent office (PTA)
  - You can get time back (up to 5 years) for regulatory delays (PTE)
- Many Universities can not absorb the cost of multiple foreign filings at 30-months
  - Investors have an expectation that technology is covered in major markets/manufacturing locations

Application	Official/Associate	Translation	In-House/Miscell.	Total
AP ARIPO	$4,447	$0	$1,142	$5,589
AU Australia	$1,363	$0	$1,142	$2,505
BR Brazil	$1,283	$7,965	$1,142	$10,390
CA Canada	$1,290	$0	$1,142	$2,432
CL Chile	$2,267	$8,215	$1,192	$11,674
CN China	$4,002	$11,381	$1,142	$16,525
CO Colombia	$2,524	$6,530	$1,192	$10,246
EA Eurasian Patent Conv.	$5,726	$10,620	$1,142	$17,488
EP European Patent Office	$11,326	$0	$1,000	$12,326
ID Indonesia	$2,567	$8,448	$1,142	$12,157
IL Israel	$1,708	$0	$1,142	$2,850
IN India	$4,698	$0	$1,142	$5,840
JP Japan	$1,476	$15,851	$1,142	$18,469
KR Korea, Republic (KR)	$884	$13,806	$1,142	$15,832
MX Mexico	$1,756	$7,392	$1,192	$10,340



Managing the Patent Clock

- If possible, do not disclose and start the clock until the technology is developed
  - This is a risk and should be assessed carefully
  - May not be a wise strategy in competitive targets and fields
- Be at the point were a license to the technology to a funded start-up or out-license to an entity that can support broad filing can be achieved within 30-months
- Some grants will support costs associated with IP which may be used to file in key jurisdictions
- If you have multiple series, consider filing multiple provisional applications
  - Advance one but don't risk disclosing back-ups until they are more developed



- University would only file in US
  - Despite a license in negotiation
- CEO managed to get an upfront payment of $150K in December to cover national filings
- Seed funding complete February 2025

Not the Patent Clock, but the dull stuff is over…

Thanks to:

Maaike Everts, Mary O'Reilly & Joanna Yang Yowler

HRA and it's members

CRITICAL PATH
INSTITUTE

Advancing Drug Development.
Improving Lives. Together.

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