Pediatric Oncology Development at BMSKK

Kiyoshi Hashigami, M.D.
Head of Research & Development, Japan/Korea/Taiwan
Bristol-Myers Squibb

July 12, 2019

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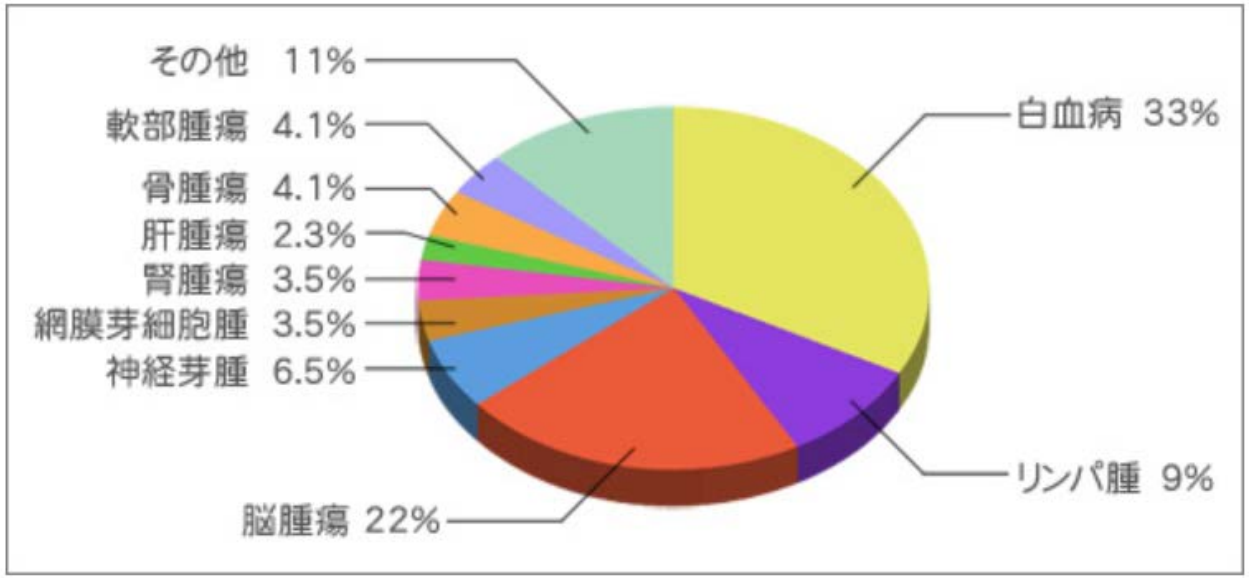
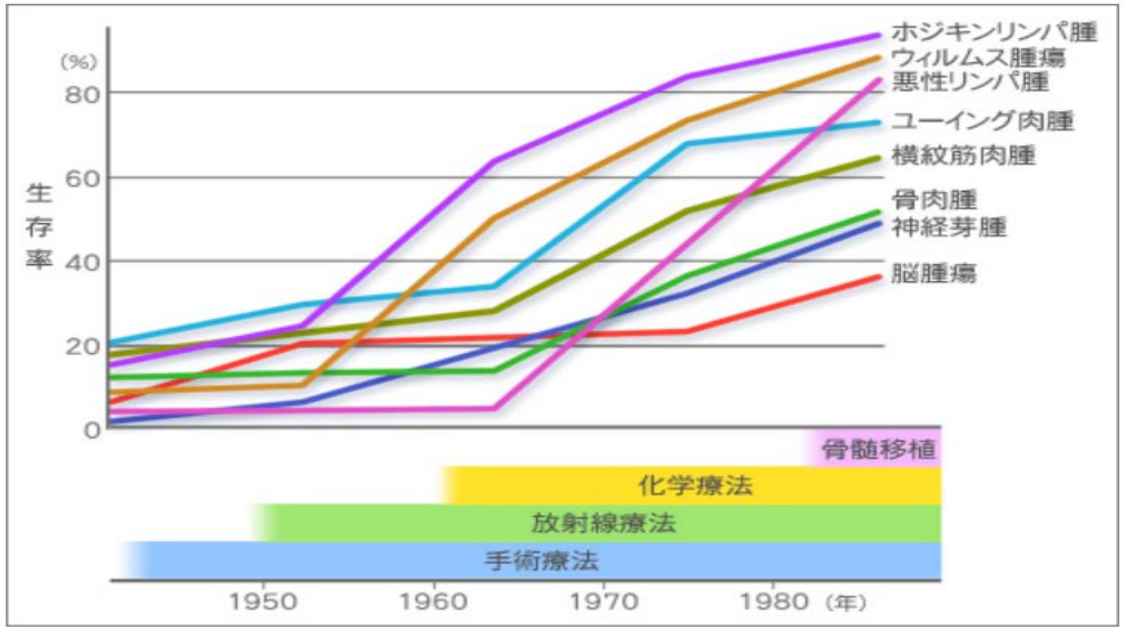
The Need in Japan is clear: ~ 2500 pediatric cancer patients per year

Japan Children's Cancer Group





- Survival rates for Japanese pediatric cancer patients is now at 70~80%
- For the remainder who relapse or who must discontinue SoC treatment, there are few treatment options, and clinical trials are often the "last hope" for this patient group

https://ganjoho.jp/child/dia_tre/about_childhood/about_childhood.html

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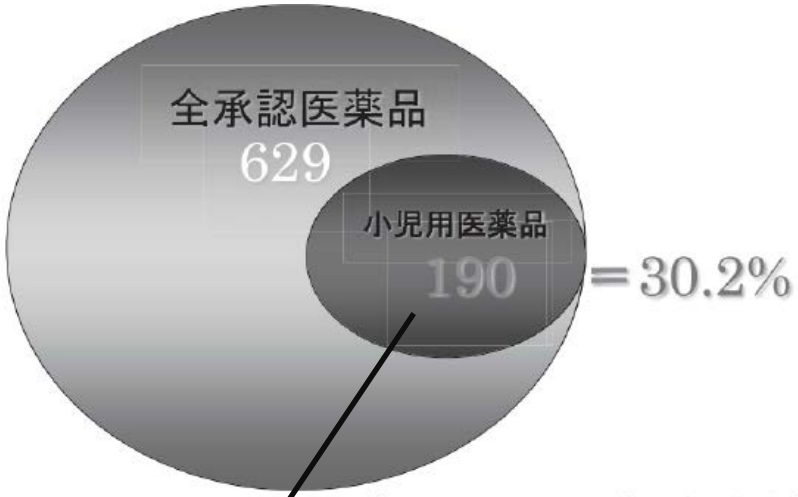
2010-2015: 30% of newly approved drugs also gained a pediatric indication, but only half of those had new pediatric trial data



医薬品医療機器総合機構HP審査報告書より

91件に治験データあり
99件は既存データの基に承認

臨床試験実施	**91品目(47.9%)・・・18.2品目/年**
ワクチン	14
アレルギー疾患治療薬	17
感染症治療薬	14
神経疾患(てんかん等)	10
膠原病・悪性腫瘍	5
その他	31(医師主導治験 1、国際共同治験6を含む)
臨床試験なし	**99品目(52.1%)**
医学薬学上公知	63 (使用実態調査実施 10)
海外データのみ	16(国内超稀少疾病等)
成人データのみ	13 (インフルエンザHA等)
製法変更	2
有効成分含有量変更	2
海外文献のみ	1
配合剤	1
後発バイオ	1

医療上の必要性の高い未承認薬・適応外薬検討会議 59

Ref: 日本小児科学会誌 第120巻 第10号

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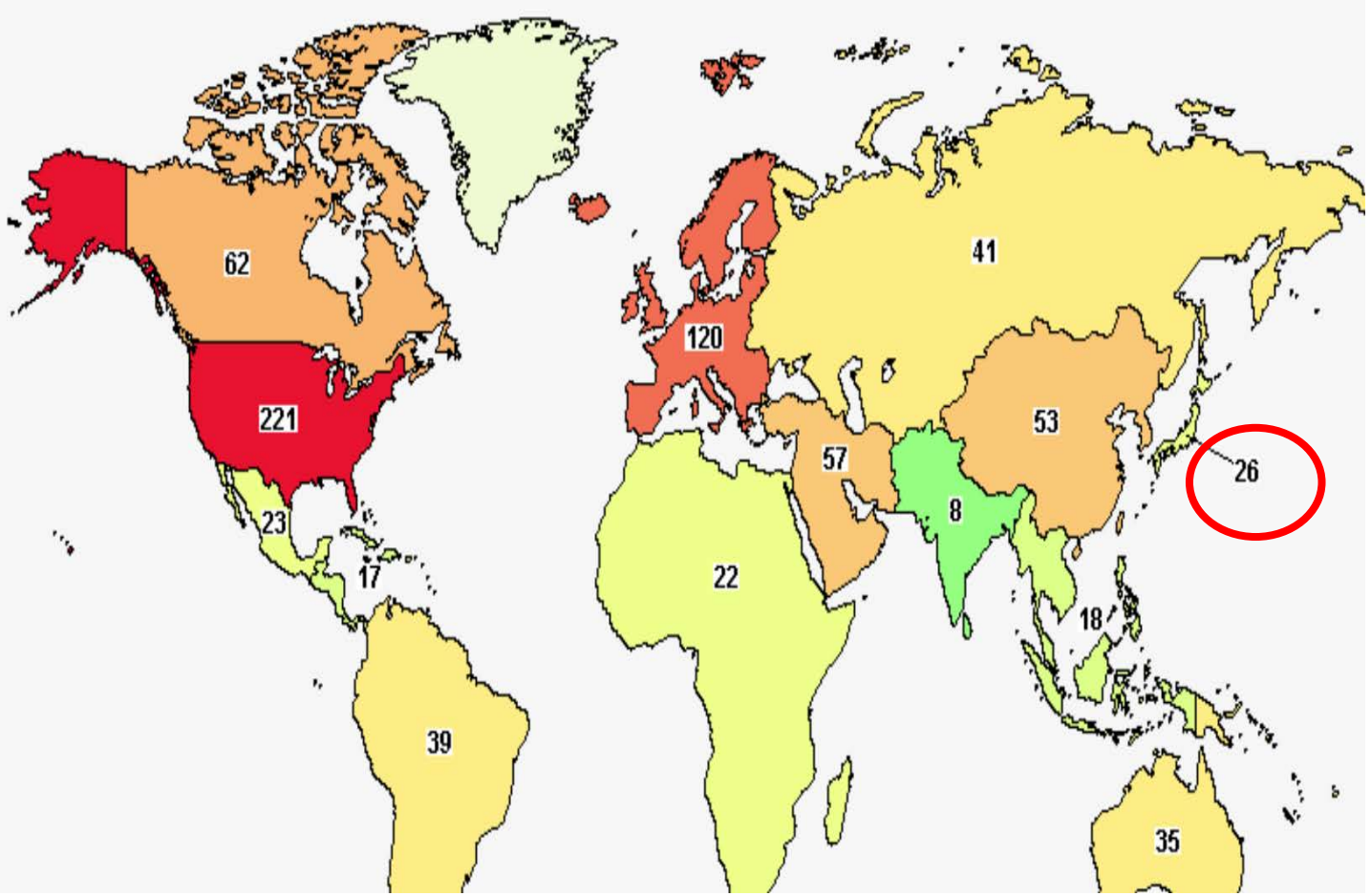
26* Industry-sponsored pediatric trials currently enrolling in Japan



Taken from
Clinicaltrials.gov search
Jun 25, 2019

Search Term: Pediatric
Funder Type: Industry
Study Status: Recruiting patients

* Author acknowledges that this ct.gov data may not represent a full picture of total trial activities; provided here as an illustrative example

https://www.clinicaltrials.gov/ct2/results/map?cond=pediatric&term=&cntry=&state=&city=&dist=&recrs=a

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Only 5 Industry-sponsored pediatric oncology trials registered in Japan

Of 26 trials, only 5 pediatric cancer trials

- Hodgkin's disease
- AML
- CML
- TRK-fusion tumors
- Gliomas

Taken from Clinicaltrials.gov search Jun 25, 2019

Search Term: Pediatric
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https://www.clinicaltrials.gov/ct2/results/map?cond=pediatric&term=&cntry=&state=&city=&dist=&recrs=a

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日本小児科学会雑誌　120巻10号　1453～1461（2016年）

日本小児臨床薬理学会推薦総説

本邦における小児医薬品開発推進のための提言

1. 小児医薬品開発の奨励と小児を対象とした臨床試験の要請（義務化）
2. 組織改革　－　小児部門、小児医薬品を検討するための公的組織の設立
3. 企業にとってのインセンティブ設定
4. 新生児を含むすべての年齢層への対応
5. データベース作成に向けたレジストリー研究の推進とアーカイブ活用
6. 治験実施体制の整備
7. 人材育成
8. 国民への啓発および患者・保護者の参画
9. 製薬企業の役割

BMS Commitment to Pediatric Oncology

Mission

BMS is committed to discover, develop and deliver safe and effective innovative medicines that help pediatric patients prevail over cancer

Priorities

1. Advance the strategic development of early assets across multiple pediatric cancers and advance preclinical research (translational medicine and biomarker)

2. Advance clinical research of IO/IO, IO/non-IO combinations and other cutting-edge technologies in pediatric cancer patients

3. Effectively address key issues that affect pediatric cancer survivors

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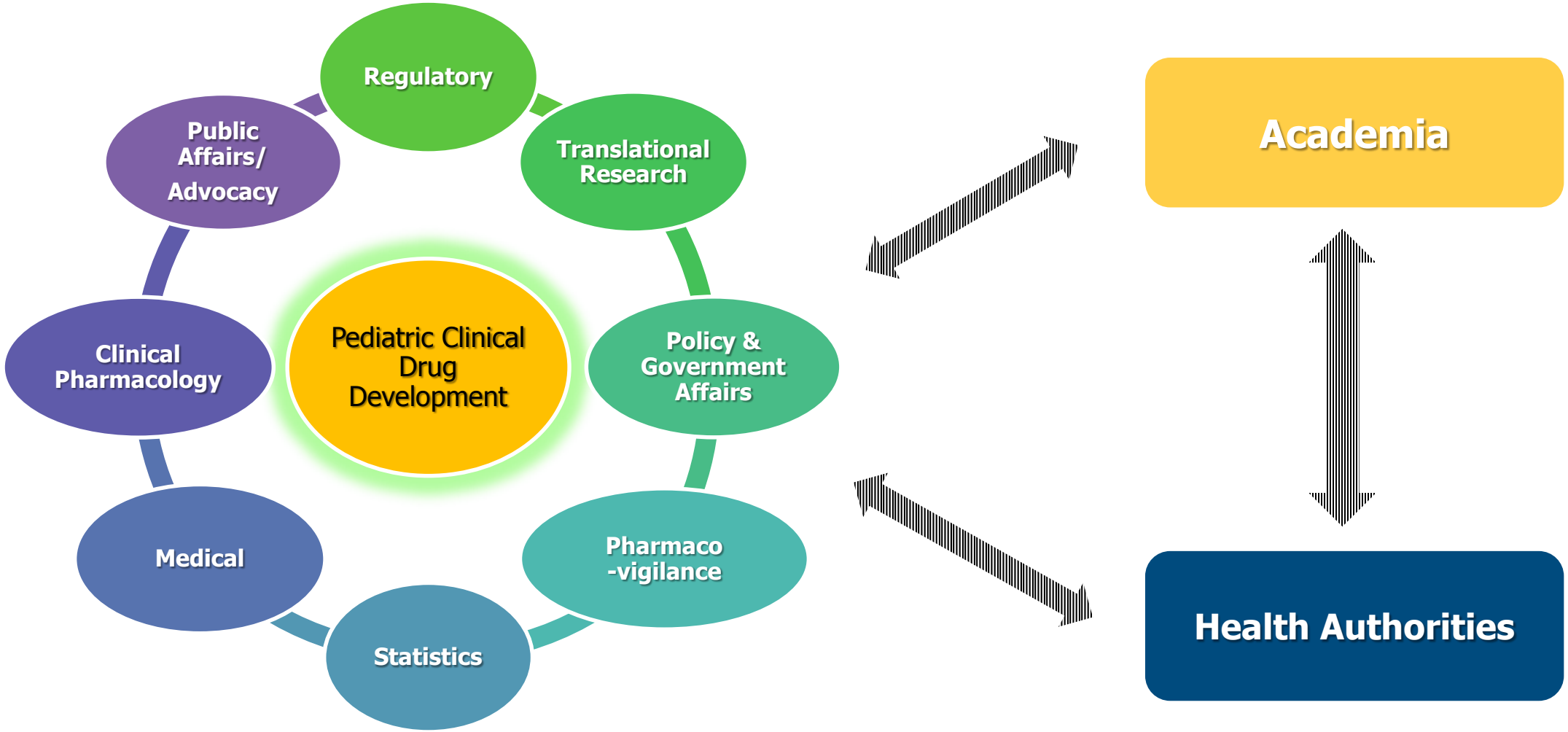
BMS has robust drug development expertise, but further optimization of the industry-regulator-academia relationship is needed



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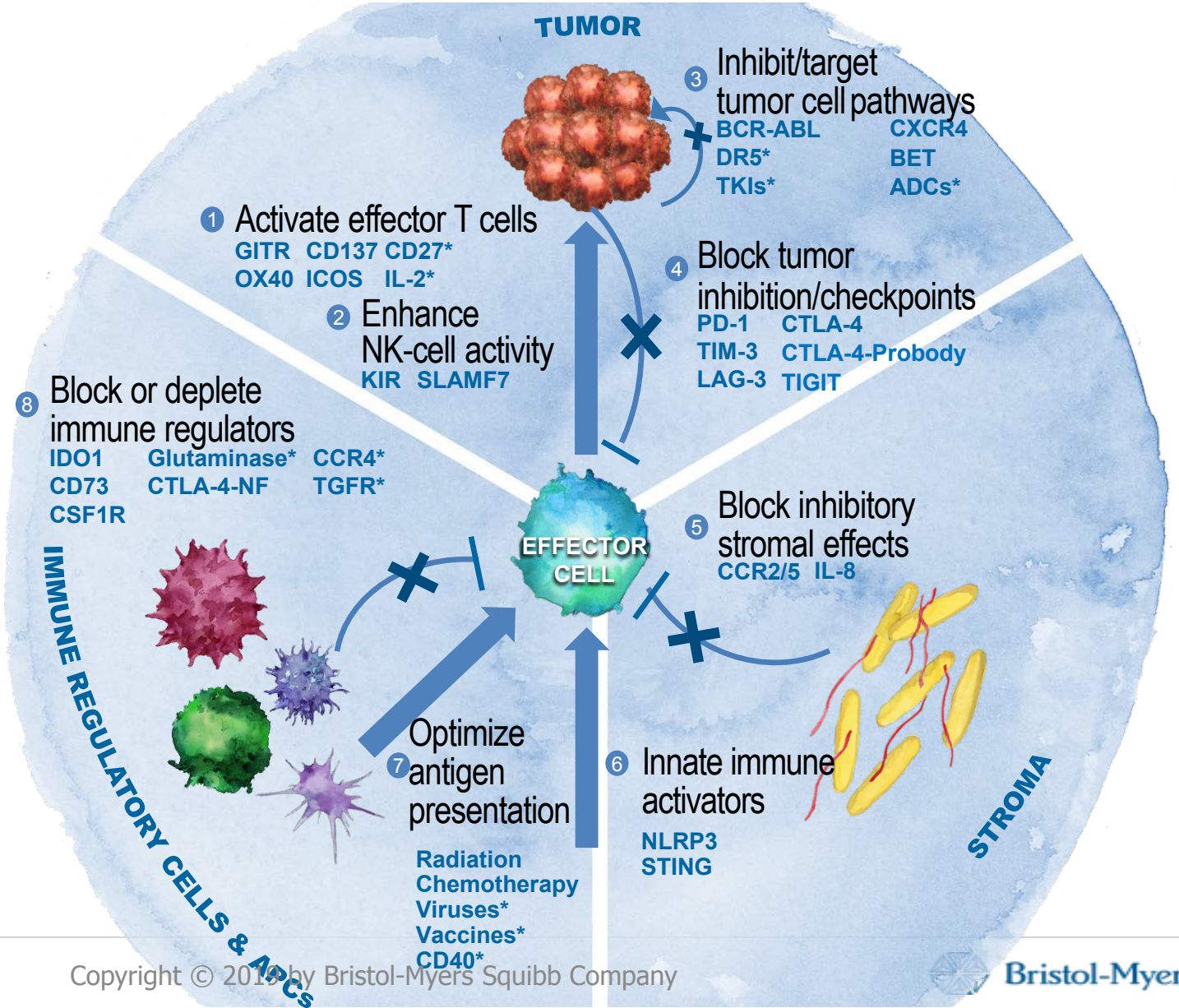
BMS Oncology Pipeline Addresses Multiple Pathways in Anticancer Immunity

BMS is developing a deep portfolio of novel clinical-stage therapies with the potential to provide transformational clinical benefits*



*Includes clinical collaborations.

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Innovative trial designs & regulatory pathways are needed: Data registry utilization as the answer?

Regulatory filing and review

Pediatric Trial Limitations

- All pediatric tumors are rare
- Clinical trials can only enroll few patients
- Need to follow long-term outcomes of patients
- Data currently not used past mandated regulatory reporting

Database registries

- Potential to use registry data as synthetic control arm (SCA), eliminating control arm of trial
- A consolidated database can follow patients on SoC, trial participants, and post-trial follow-up patients indefinitely
- Best-practice sharing on treatment outcomes. AE management possible with current technology

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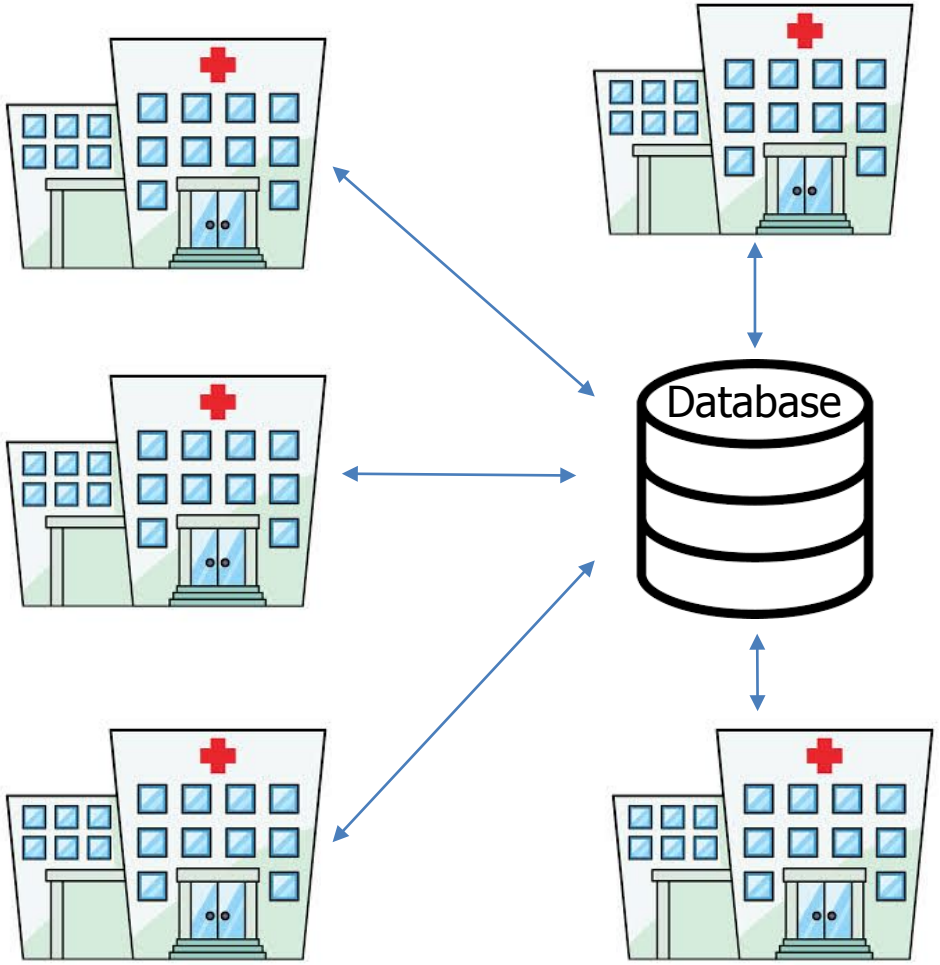
Modern Database Capabilities offer technological innovations to address widely recognized limitations



State-of-the-art database platforms have ability for:

- AI-assisted automated data input directly from hospital EHR
- Ability to unify multiple EHR systems into one structured database
- Data privacy concerns mostly resolved in major global markets
- Real-time data sharing – ability to share best practices and treatment outcomes, including AE management
- Long term follow-up possible for all patients

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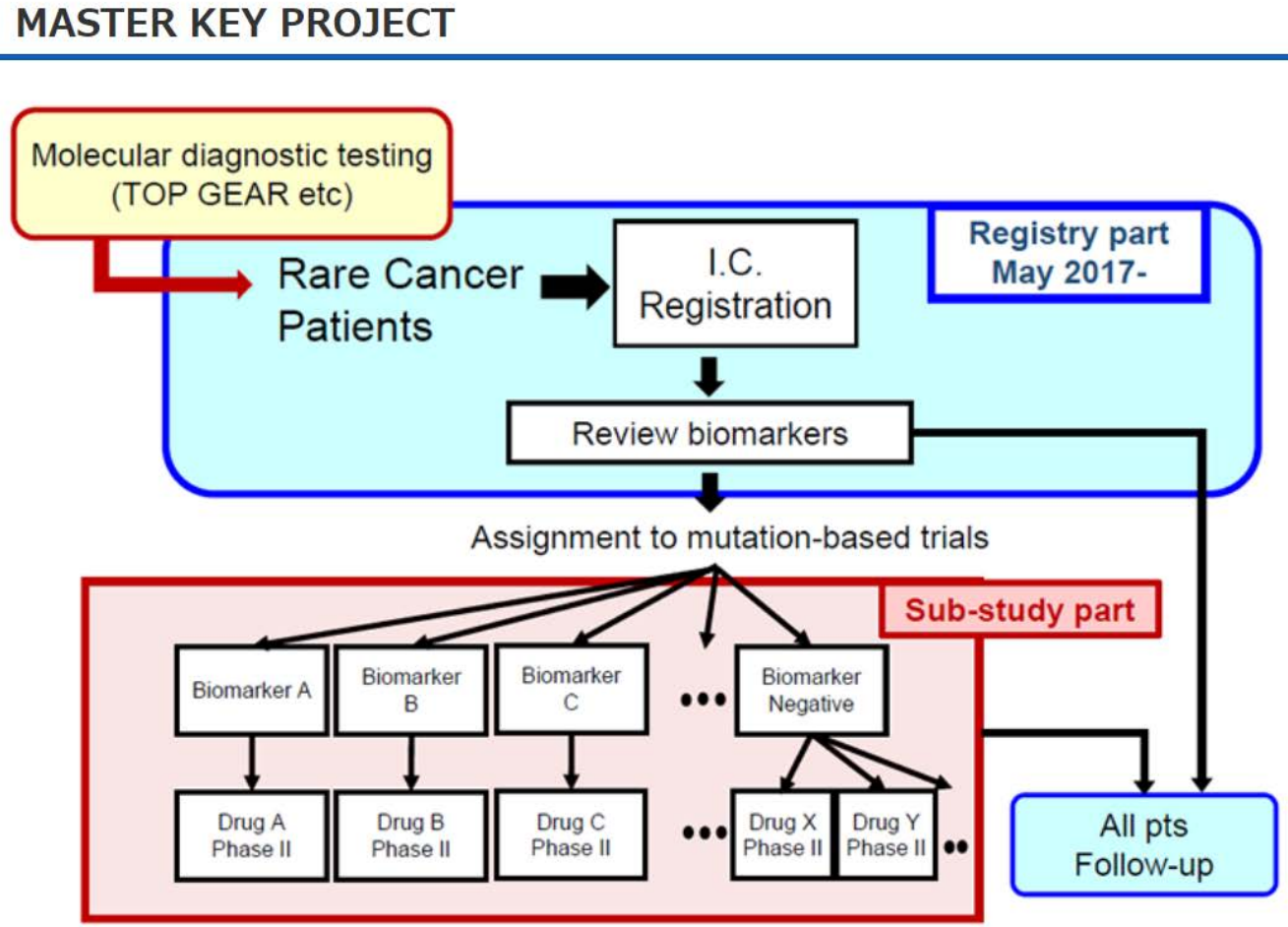
National Cancer Center's Master Key Project addresses development challenges in rare tumors



Strengths:

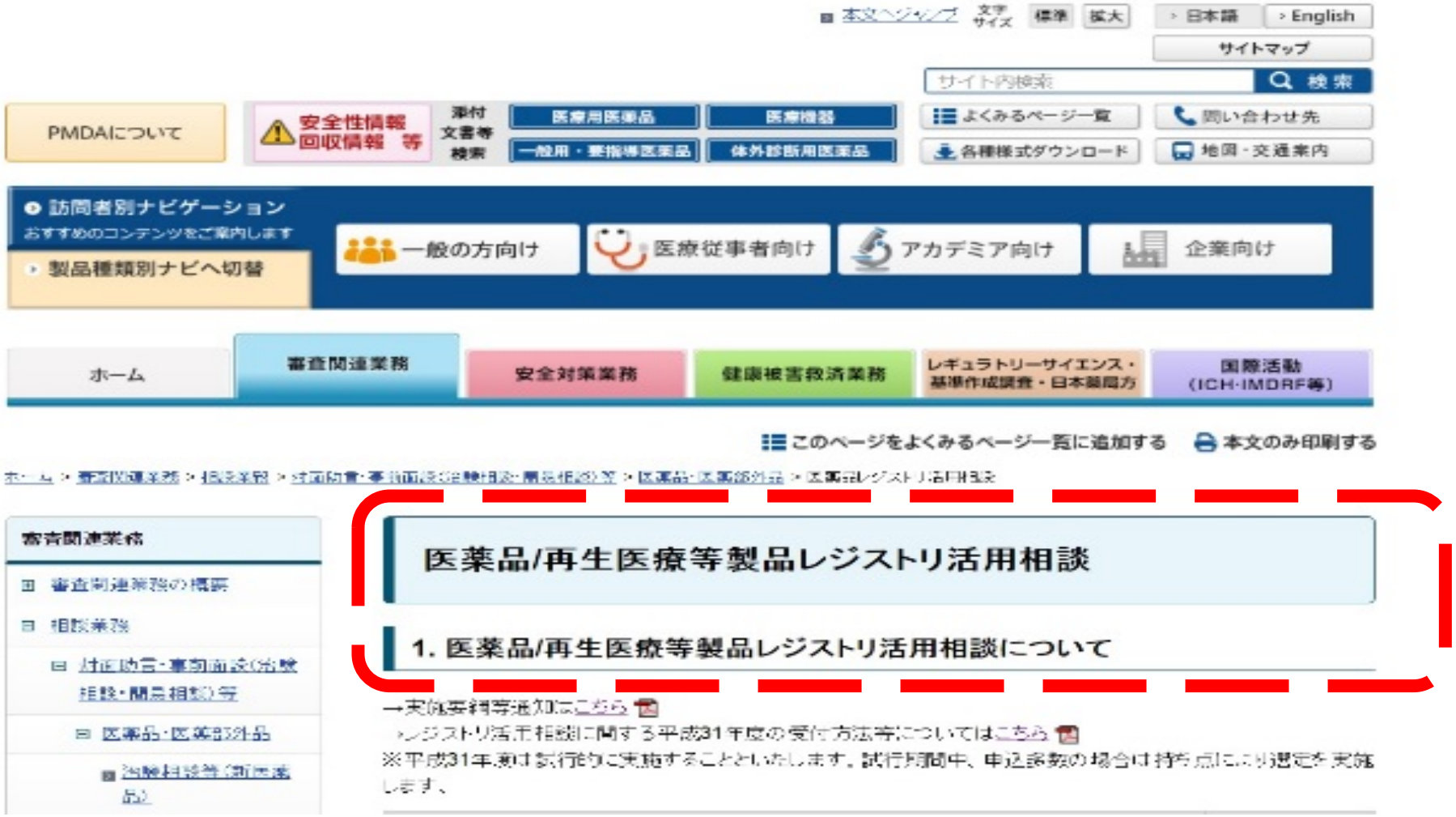
- Umbrella / basket trial design with ability to add new trial arms
- Parallel enrollment in data registry
- Well-suited for tumors with targetable driver oncogenes
- As a part of this program, BMSKK aims to explore pipeline portfolio in this trial framework

Under BMSKK consideration:

- How suited is this trial framework to immuno-oncology drug development?
- How can the registry data be shared / utilized across institutions and investigators?
- Can registry data be used to share practice and treatment outcomes?

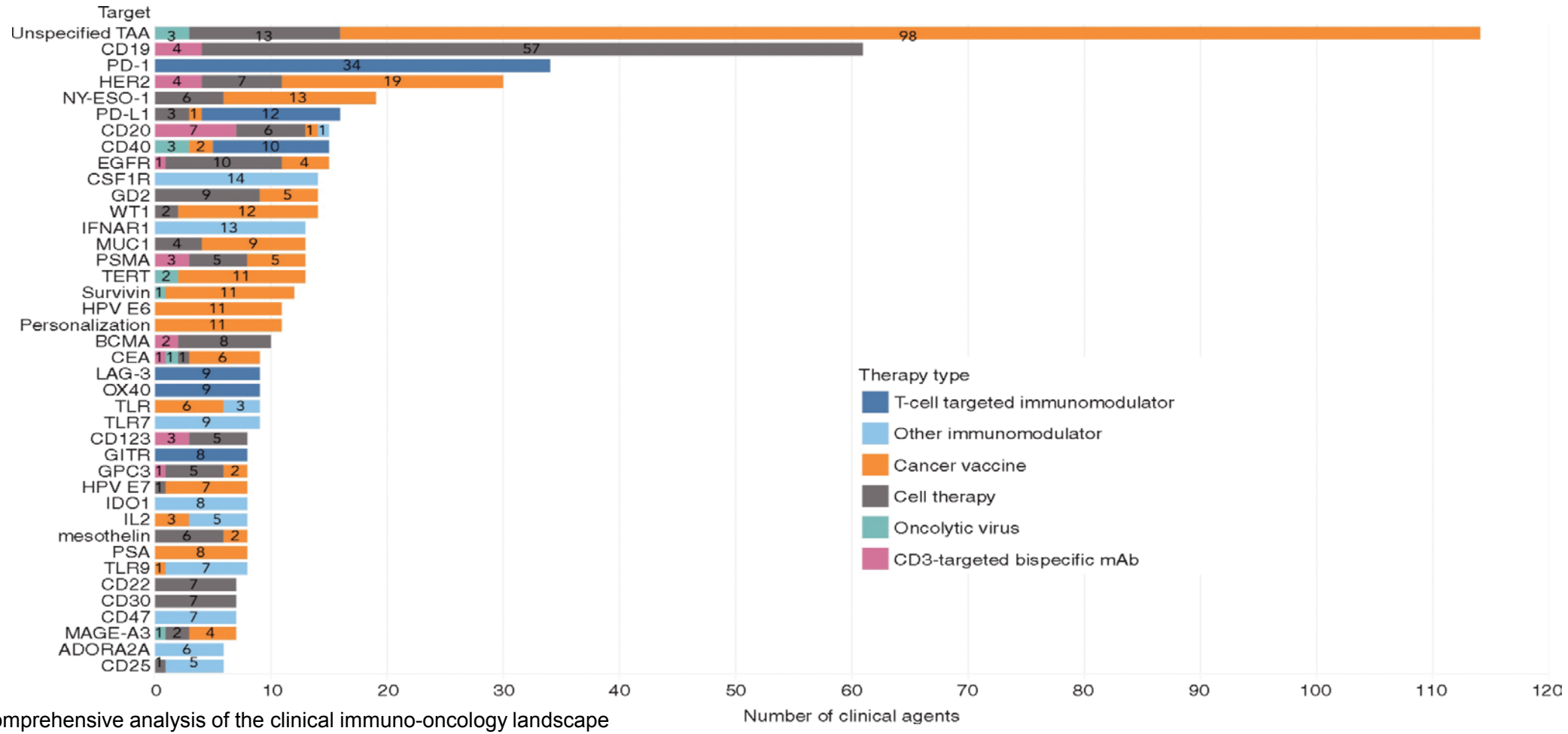
https://www.ncc.go.jp/jp/masterkeyproject/outline/overview/master_key_project_overview.html

The PMDA's Registry Utilization initiative is a welcome regulatory advancement for rare tumor drug development



https://www.pmda.go.jp/review-services/f2f-pre/consultations/0101.html

BMS has a robust oncology asset portfolio focused on immune-modulating mechanisms, but what could we accomplish if we focus collaborative industry resources on pediatric disease?



From: Comprehensive analysis of the clinical immuno-oncology landscape
Ann Oncol. 2017;29(1):84-91. doi:10.1093/annonc/mdx755

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Becoming a Frontier in Pediatric Drug Development

Bristol-Myers Squibb K.K.

Our Goals are:

- **Join BMS global pediatric trials** to accelerate pediatric drug development and access to innovative medicines in Japan, starting with an oncology focus
- **Build productive partnerships** with pediatric academic / research societies
- **Leverage advanced technology** and infrastructure of Japan for innovative drug development in pediatric oncology

Bridging key components across regions and partnership for pediatric cancer patients

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Summary

- The need for increased pediatric drug development activity is clear in Japan, especially in pediatric oncology
- Although clinical trials are an important treatment option for patients with difficult disease, Japan greatly lags behind first-world peers in pediatric clinical trials
- The difficulty of pediatric clinical trials is a globally recognized and complex problem
- BMS believes that progress can be made on the industry-side with dedicated staff, expertise, and an asset portfolio to explore against pediatric diseases
- Registry data utilization is becoming more important, especially for rare tumors – the external environment (regulators, academia) is also considering this approach
- Pediatric oncology drug development is a globally difficult problem that demands industry-academia-HA collaboration for impactful change

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Thank You

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