ANGELES THERAPEUTICS

Simplicity is the ultimate sophistication

Leonardo Da Vinci

Introduction

Current Chimeric Antigen Receptors (CARs) lack physiological regulation and resemble an "Emperor without Clothes.“

All the major limitations of the CAR-T (e.g., lack of efficacy in solid tumors, disease relapse in blood cancers, toxicities and risk of secondary T cell cancers) are primarily due to a flawed CAR design.

CAR-T field has been attributing the above limitations to factors other than the CAR design.

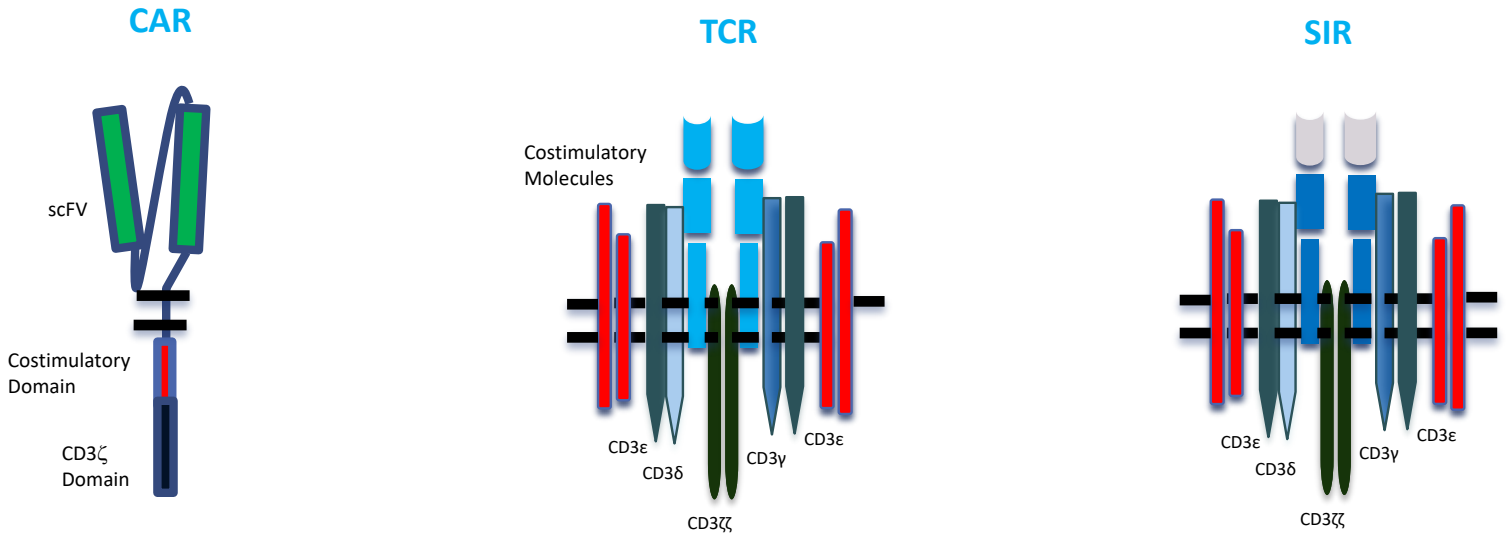
This misdiagnosed has led to significant wasted time, effort and capital, and created a unique opportunity.

Angeles recognized flaws in current-gen CAR-T design nearly a decade ago.

Angeles operated in a semi-stealth mode to create a dominant position in next gen cell therapy

SIR-T (Synthetic Immune Receptor) Platform

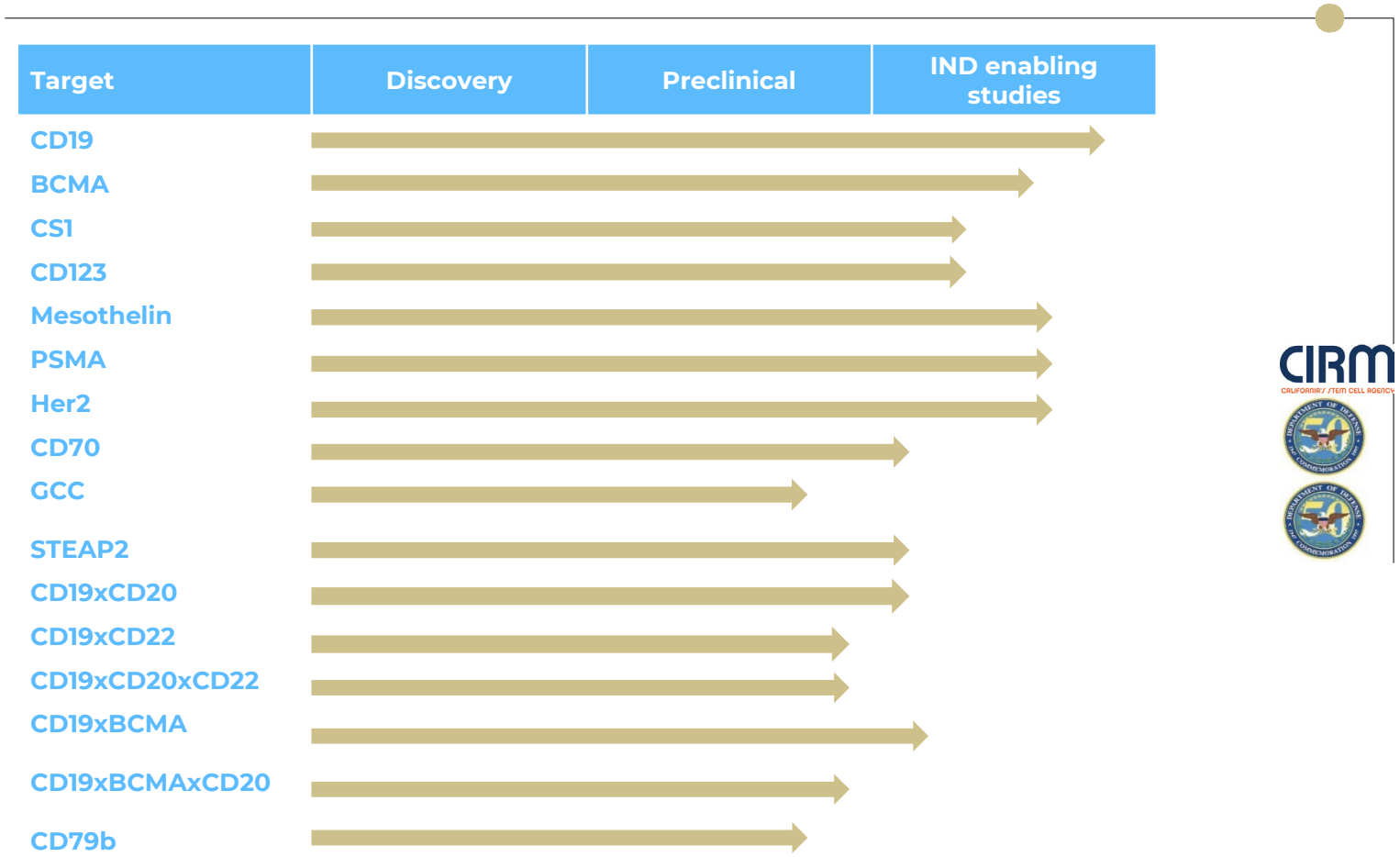
- Hybrid of T cell receptor (TCR) and CAR.
- Signals like a natural TCR, attacks cell surface antigens like a CAR – combines **best features of both**.



SIR-T Platform Advantages

- **1. Efficacy:**
  - Nearly 100% *in vivo* efficacy in multiple solid tumor models.
- **2. Durability:**
  - Physiological T cell signaling results in long-term persistence of SIR-T cells
  - Can target multiple antigens with a single receptor, overcoming disease relapse.
- **3. Safety:**
  - Low risk of cytokine release, neurological complications, and secondary T cell cancers.
- **4. Cost Reduction:**
  - Potential for outpatient administration without prior chemotherapy.
- **5. Manufacturing Ease:**
  - Compatible with off-the-shelf allogeneic approach.
- **6. External Validation:**
  - 7 projects with >$10M in peer-reviewed funding from CIRM and Department of Defense.
  - Validation by big pharma under MTA
- **7. Deep Pipeline:**
  - Numerous assets advancing toward Investigational New Drug (IND) filing.
- **8. Dominant IP Position:**
  - >150 patent applications pending worldwide.
- **9. Flexibility:**
  - Open to various investment/partnership models
    - New company formation around selected assets
    - Out-licensing
    - Co-development partnerships
    - JV

Winning *Lead SIR-T* programs



CIRM and DoD grant funding was provided to Preet Chaudhary, MD, Ph.D. laboratory at U.S.C

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Extensive *Pipeline SIR-T* Programs

Target	Discovery	Preclinical	IND enabling studies
FOLR1			
EGFRviii			
ROR1			
GD2			
IL13Ra2			
CLDN-18.2			
CLDN6			
PSCA			
B7-H3			
CD30			
CD33			
GPRC5D			
GPRC5D x BCMA			
Her2 x IL13Ra2			
STEAP1			

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CAR-T vs SIR-T

Property	CAR-T	SIR-T
Toxicity	Yes	**No**
Non-physiological tonic signaling	Yes	**No**
T cell exhaustion	Yes	**No**
Lack of persistence	Yes	**No**
Disease relapse	Yes	**No**
Lack of efficacy against solid tumors	Yes	**No**
Immunogenicity	Yes	**No**

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Unique Investment/Partnership Opportunities

- **Unique Offering:**
  - Largest portfolio of next-gen cell therapies globally.
  - Several assets ready for IND filing in the next 6-12 months

- **Flexibility:**
  - Open to various investment/partnership models
    - New company formation around selected assets
    - Out-licensing
    - Co-development partnerships
    - JV

- **Leapfrogging Opportunity:**
  - A partnership with Angeles enables leapfrogging established cell therapy companies facing traditional CAR-T limitations and new regulatory challenges due to recently identified risk of secondary T cell cancers .

Angeles ecosystem for cell therapy

Proprietary Synthetic Immune Receptor-T (SIR-T) and SIR-NK and U-SIR (Universal) platforms

Superior efficacy against solid tumors and blood cancers *

Safe

Lead pre-IND programs
PSMA
Mesothelin
Her2
CD70
CLDN6
STEAP2

Underpinned by 15 patent families owned or exclusively licensed from USC

>150 patent applications granted or pending

Global protections covering 60 regions/territories

Advanced pipeline
CD19
BCMA
CD123
GD2
CD19 x CD22
CD19 x CD22 x BCMA

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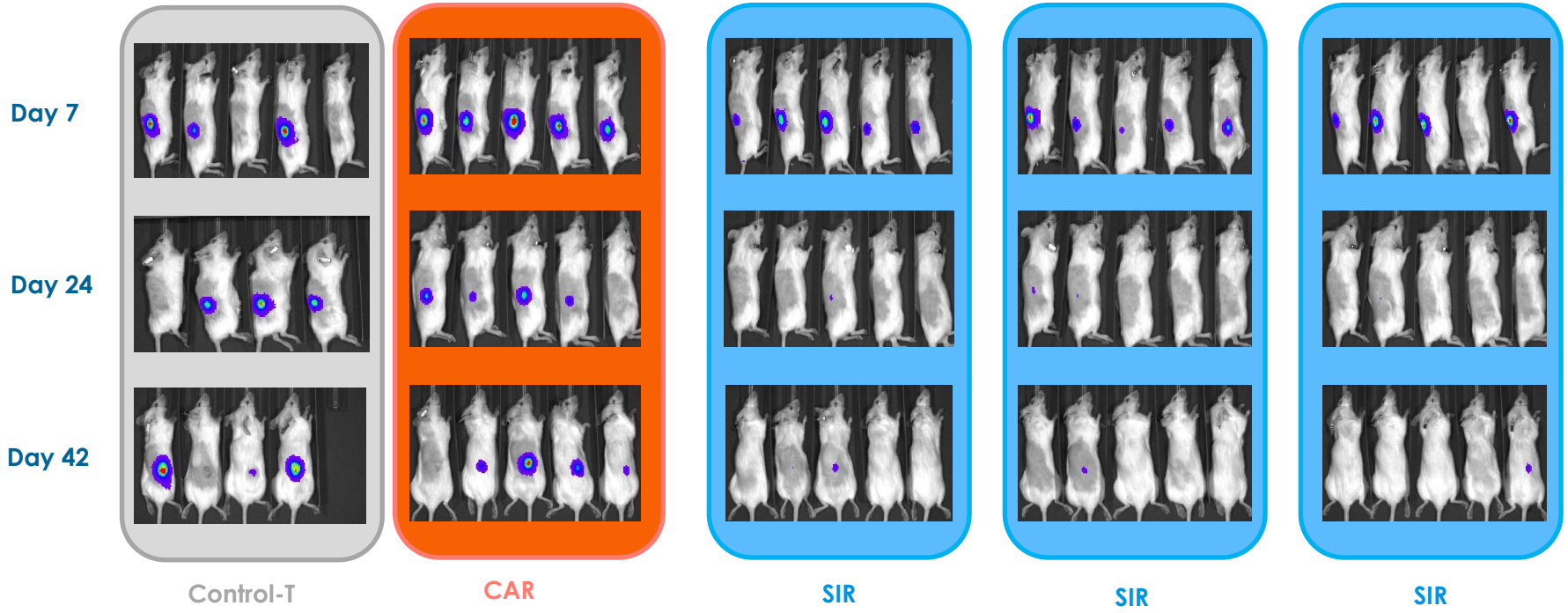
SIR-T overcomes the lack of efficacy of CAR-T in solid tumors: *Ovarian cancer xenograft model*



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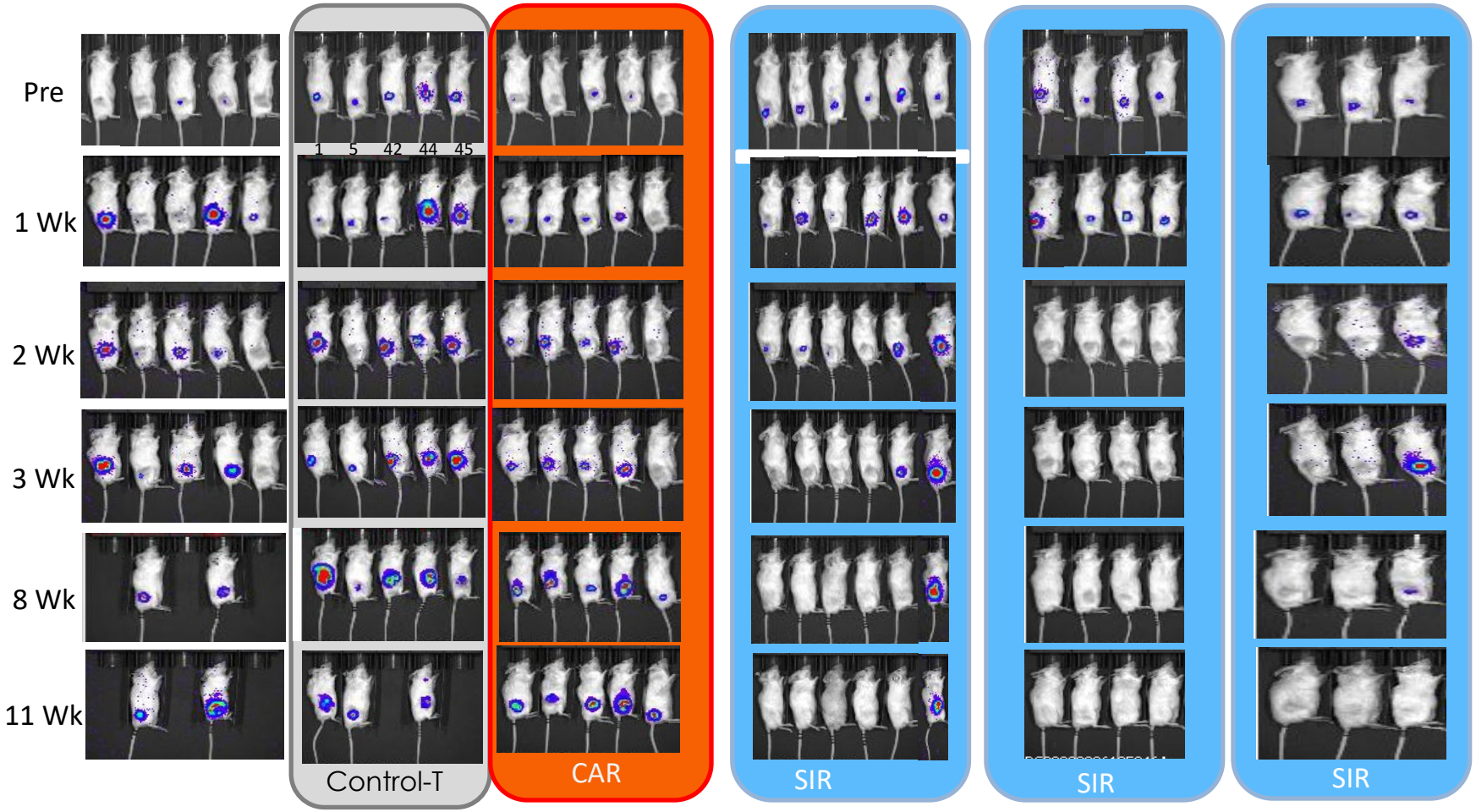
SIR-T overcomes the lack of efficacy of CAR-T in solid tumors: *Prostate Cancer Xenograft Model*



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Recent Peer-Reviewed Funding *

- SIR-T targeting **melanoma**
- SIR-T targeting **kidney cancer (2022)**
- SIR-T targeting **kidney cancer (2023)**
- Bispecific-SIR-T asset targeting **lymphoma**
- SIR-T targeting **prostate cancer**
- **SIR-T targeting ovarian cancer**

CIRM
CALIFORNIA'S STEM CELL AGENCY

- SIR-T asset targeting **prostate cancer**

- ~$ 10.0 M in non-dilutive funding to accelerate 7 lead programs.
- Grant funding was provided to Preet Chaudhary, MD, Ph.D. laboratory at U.S.C.

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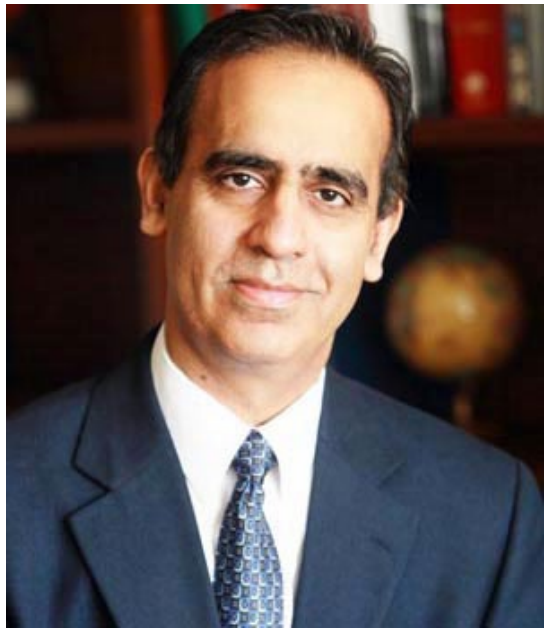
Founder's Track Record of Success

Highest cited cancer related patent in the world between 1993 and 2013



Preet M. Chaudhary, MD, PhD

Founder

Professor and Chief of Hematology and Director of Blood and Marrow Transplant and Cell Therapy at University of Southern California

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PLOS ONE

Clearing the Fog of Anticancer Patents from 1993–2013: Through an In-Depth Technology Landscape & Target Analysis from Pioneer Research Institutes and Universities Worldwide

Ajay Dara, Abhay T. Sangamwar*

Department of Pharmacoinformatics, National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Punjab, India

Citing patent analysis. The patent with maximum citing count is considered as the core technology, as many inventor/assignees are working in the same field of technology and the work is assumed to be actively performed based on number of forward citation. The PCT application WO1999011791A2 with a count of 168 citation has been reported as the top citing patents assigned to University of Washington with only one inventor Chaudhary Preet M. The patent was published in year 1999 claiming the priority year 1997 and talks about the invention related to the new tumour necrosis factor (TNF) family receptor polypeptides and ligands useful for diagnosis and treatment of prostate cancer and developmental or gestational abnormalities [34]. The novelty of the invention claims the isolated TNF polypeptides: apolipoprotein APO4, APO6, APO8 and APO9 along with the isolated TNF related ligands 1 and 3 (TNRL1 and TNRL3) and their active fragments. This patent has been cited much by the Human Genome Sciences, Inc. followed by the Smithkline Beecham Corporation; Genentech, Inc; Biogen Idec Ma Inc; The Uab Research Foundation and Zymogenetics, Inc. which are considered as the active assignee in the field of TNF anticancer targeted drug discovery (Figure 7).

Non-patent citation analysis. The study would analyse the number of non-patent documents such as review/research articles,

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