CAR-T cell therapy: Case study

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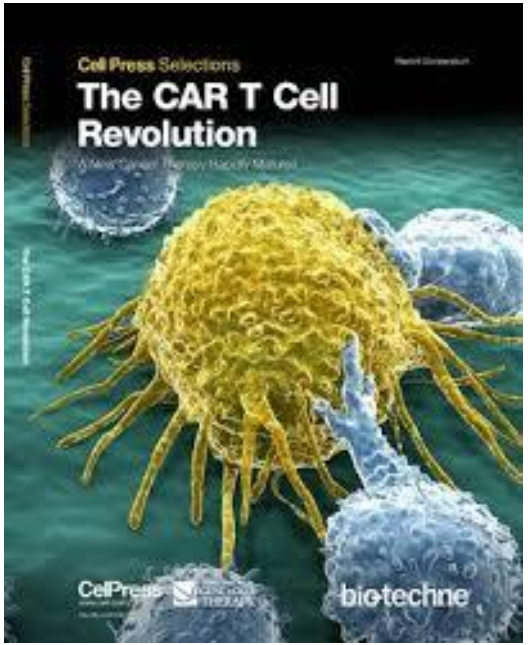
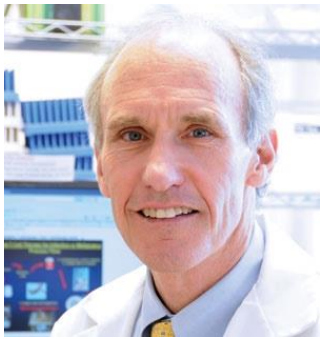
Founder - ImmunoACT

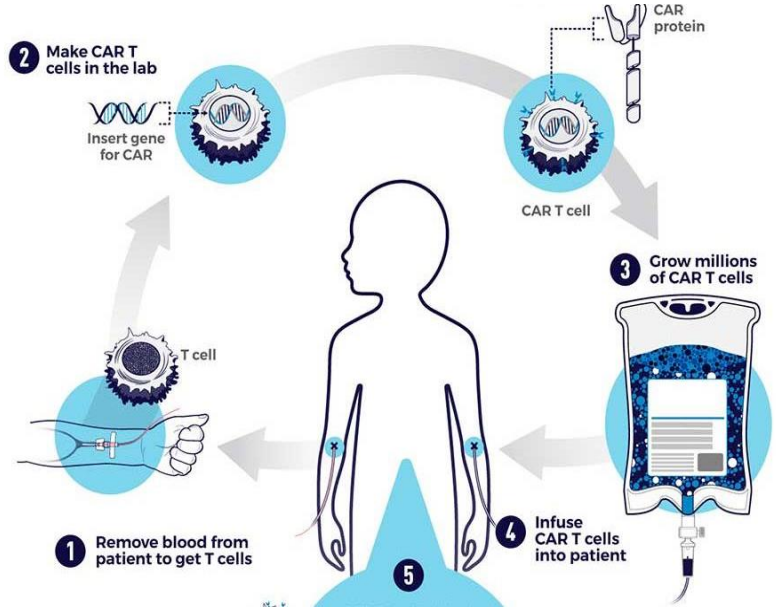
10 June 2024

Honorable President of India launched India's first CAR-T cell therapy

CAR-T cell therapy: Cell & Gene therapy





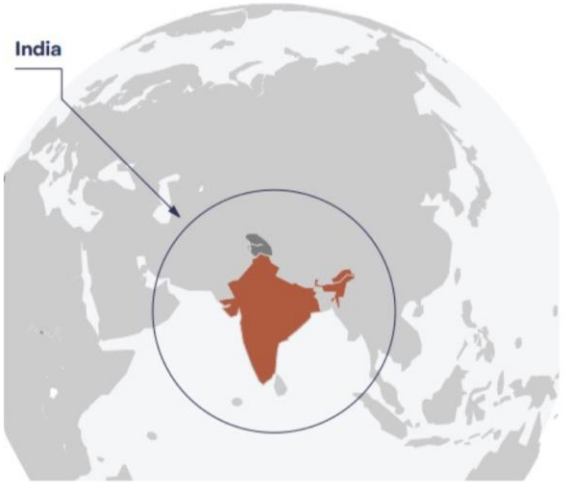


CAR-T cell therapy: An Intent-to-Cure platform

Indian Context: CAR T Therapy access

- ~20,000 cases need CAR T-cell therapy per year
- BMT story in India
- 100+ centres; <5% in need get a transplant

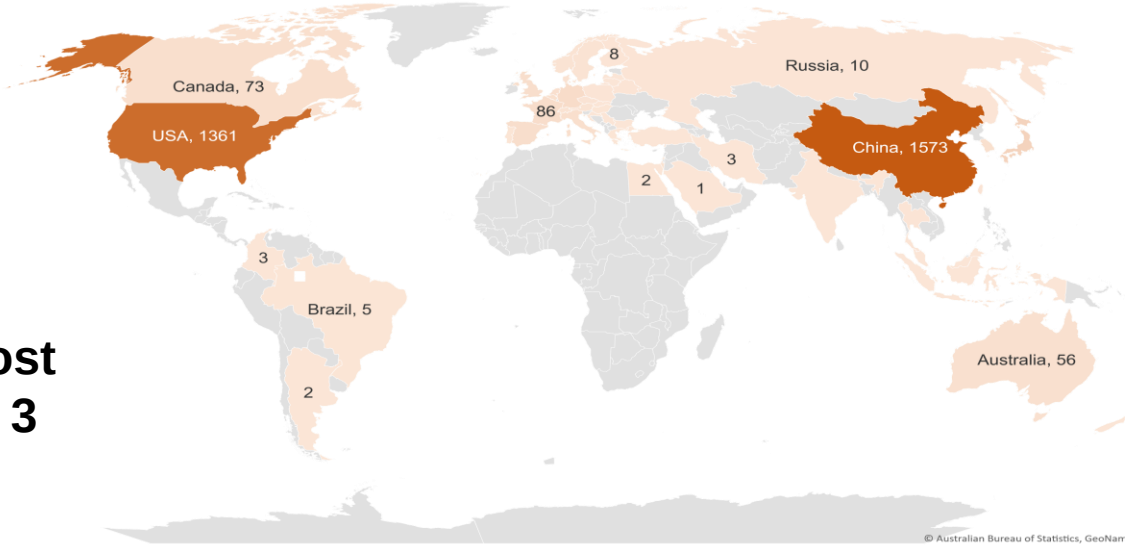
NHL and Leukemia cases ~ 100,000/year*



Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today, accessed [11/04/2024]
Hematopoietic cell transplantation landscape in India. Medical Journal Armed Forces India. 2023 Sep 13.

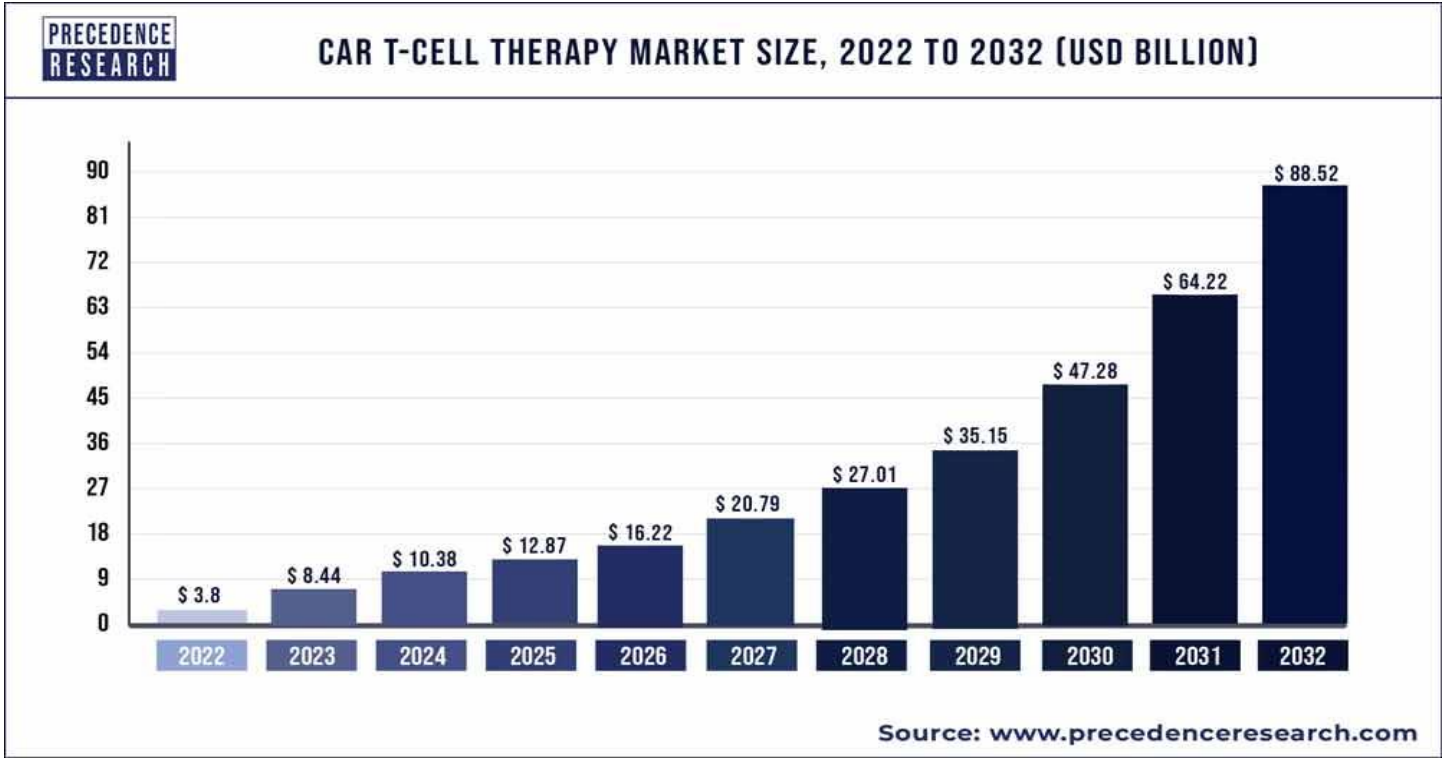
Patients in India do not have “access” of “curative platform/technologies” due to high cost

- **Global; demand-supply mismatch**
- **Huge unmet need**
- **The major obstacle is cost (Approx. $ 0.5 million to 3 millions USD /patient**

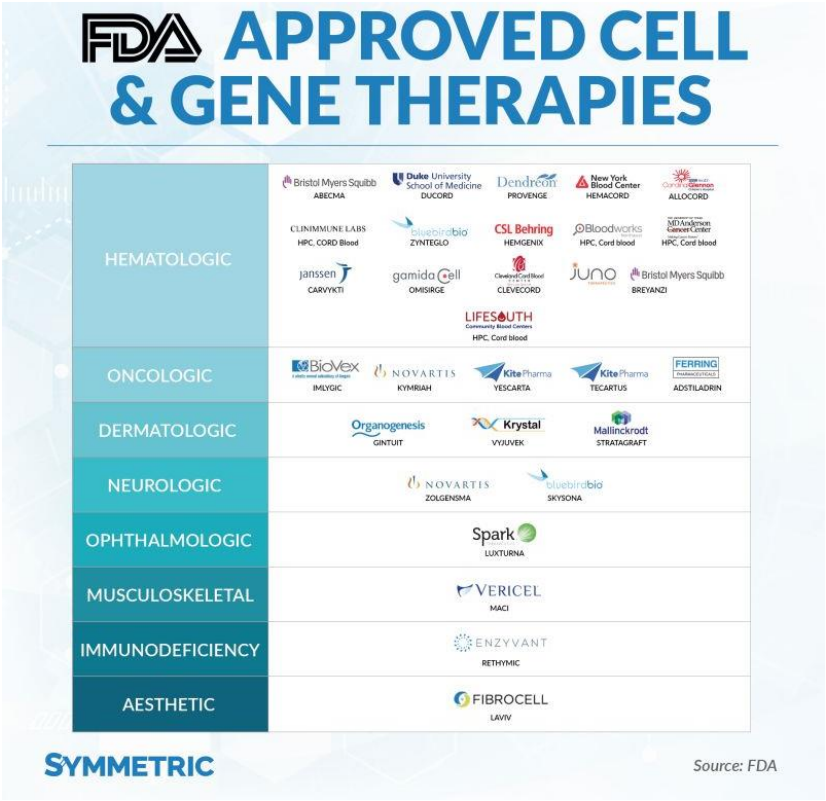


Availability in global north

Opportunity: This is just CAR-T, Cell & gene therapy is HUGE



India: Just got it First gene therapy approved (Oct 2023)



Approved Global CAR-T Therapies

$475,000

$375,000

$373,000

$410,300

$437,968

$465,000

US List Prices

Innovation is the key to affordability and improving access

Slide taken from Dr Hasmukh Jain presentation

Lower cost doesn’t mean low quality

Same price- 300 USD; Same hotel chain; But notice the difference

Fairfield Inn, Marriott,
New york

St.Regis, Marriott , Mumbai

Slide taken from Dr Hasmukh Jain presentation

Our Objective

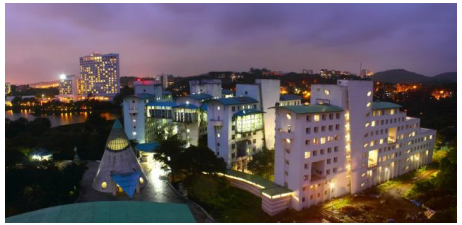
Improving access of CAR-T cell therapy

- Affordable (Cost reduction by 10x)
- Scale

Our efforts: creating " Ecosystem" for "first-in-India" CAR-T therapy

Our Journey to Create Affordable CAR-Ts (2003-2023)

IIT Bombay



- Product and Technology development

Dr Gaurav Narula

TMH

- Clinical studies / clinical trial

Dr Hasmukh Jain

NCI, USA

- Knowledge Partner (subject matter expertise)

Dr Nirali Shah

ImmunoACT

- Clinical translation

Dr Terry Fry

Dr Steven Highfill

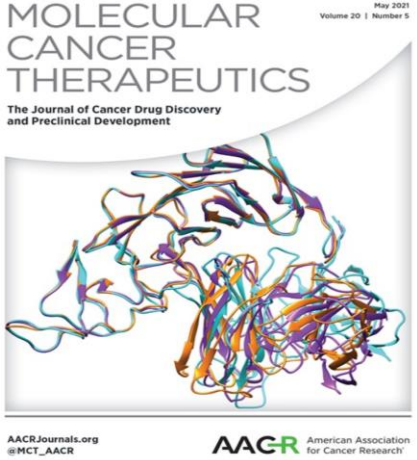
Pre-clinical Studies

Robust Antitumor Activity and Low Cytokine Production by Novel Humanized Anti-CD19 CAR T Cells

Alka Dwivedi[1], Atharva Karulkar[1], Sarbari Ghosh[1], Srisathya Srinivasan[1], Bajarang Vasant Kumbhar[2], Ankesh Kumar Jaiswal[1], Atish Kizhakeyil[1], Sweety Asija[1], Afrin Rafiq[1], Sushant Kumar[1], Albeena Nisar[3], Deepali Pandit Patil[3], Minal Vivek Poojary[4], Hasmukh Jain[3], Shripad D. Banavali[3], Steven L. Highfill[5], David F. Stroncek[5], Nirali N. Shah[6], Terry J. Fry[7], Gaurav Narula[3], and Rahul Purwar[1]

ABSTRACT

Recent studies have described the remarkable clinical outcome of anti-CD19 chimeric antigen receptor (CAR) T cells in treating B-cell malignancies. However, over 50% of patients develop life-threatening toxicities associated with cytokine release syndrome which may limit its utilization in low-resource settings. To mitigate the toxicity, we designed a novel humanized anti-CD19 CAR T cells by humanizing the framework region of single-chain variable fragment (scFv) derived from a murine FMC63 mAb and combining it with CD8α transmembrane domain, 4-1BB costimulatory domain, and CD3ζ signaling domain (h1CAR19-8BBζ). Docking studies followed by molecular dynamics simulation revealed that the humanized anti-CD19 scFv (h1CAR19) establishes higher binding affinity and has a flexible molecular structure with CD19 antigen compared with murine scFv (mCAR19). *Ex vivo* studies with CAR T cells generated from healthy donors and patients with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL) expressing either h1CAR19 or mCAR19 showed comparable antitumor activity and proliferation. More importantly, h1CAR19-8BBζ T cells produced lower levels of cytokines (IFNγ, TNFα) upon antigen encounter and reduced the induction of IL6 cytokine from monocytes than mCAR19-8BBζ T cells. There was a comparable proliferation of h1CAR19-8BBζ T cells and mCAR19-8BBζ T cells upon repeated antigen encounter. Finally, h1CAR19-8BBζ T cells efficiently eliminated NALM6 tumor cells in a preclinical model. In conclusion, the distinct structural modification in CAR design confers the novel humanized anti-CD19 CAR with a favorable balance of efficacy to toxicity providing a rationale to test this construct in a phase I trial.



Our Discovery Research, Process Development, & Clinical Manufacturing in India

Unique

Humanized anti-CD19 CAR construct

Gene delivery 3rd Gen lentiviral vector system

Tested

In vivo efficacy, toxicity and tumorgenicity

Ex vivo in healthy & r/r B-ALL patients

Patented

3 patents

FTO suggest no infringement of existing patents

First to Clinic

Kymriah, Yescarta, Tecartus, Breyanzi not available in Indian market.
No other product

Cut-price CAR-T cell therapies top India's biotech agenda

NATURE BIOTECHNOLOGY | VOL 37 | DECEMBER 2019 | 1385–1393 |

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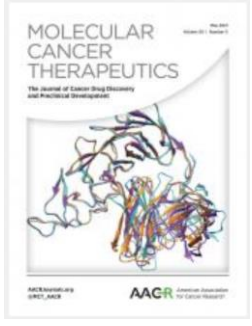
Large Molecule Therapeutics

Robust Antitumor Activity and Low Cytokine Production by Novel Humanized Anti-CD19 CAR T Cells

DOI: 10.1158/1535-7163.MCT-20-0476 Published May 2021



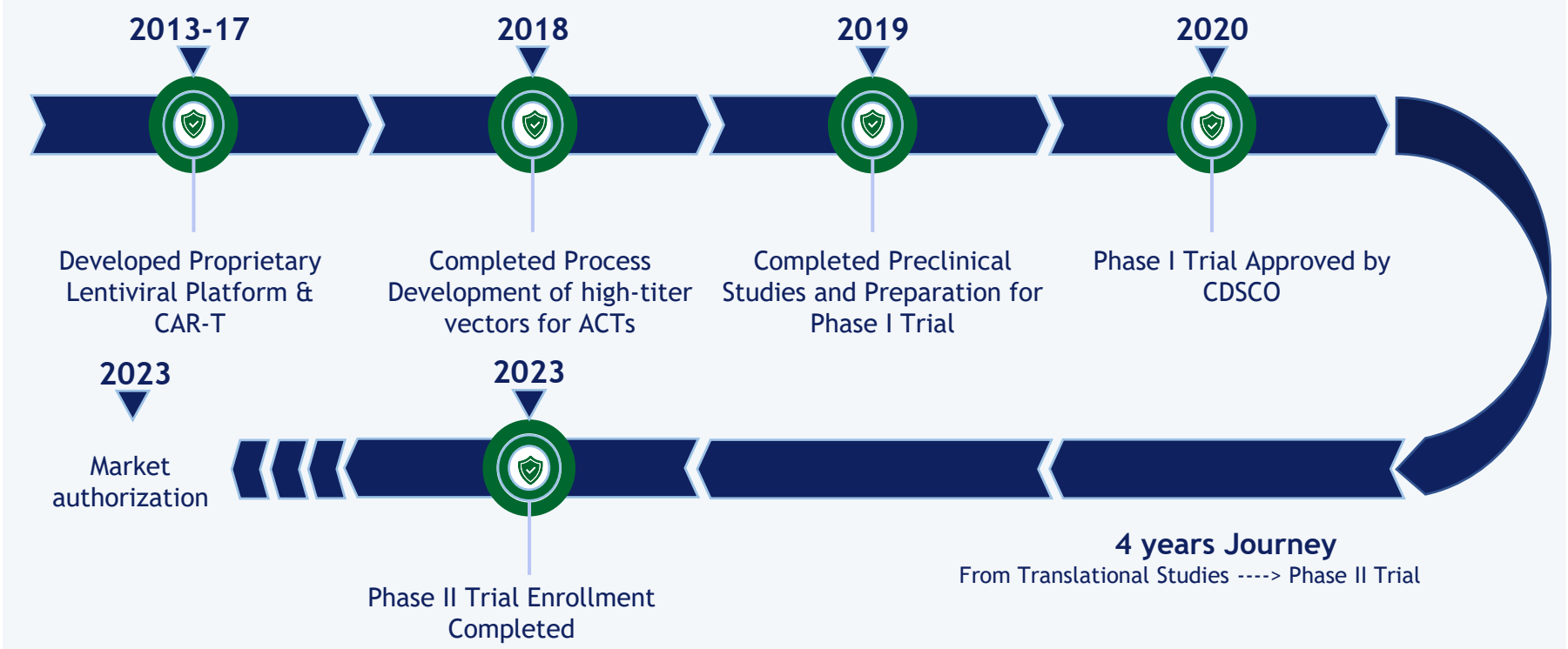
Phase I (r/r lymphoma) (adolescent and adult)

Highly safe & robust

- 150+ patients treated
- ~ 70 % response rate
- Low toxicity

30th June 2021: Dr. Hasmukh Jain and his team infused CAR T cells in first lymphoma patient

NexCAR19 : A decade in Development



*Subject to Regulatory Approvals in India

Distribution Model in India & Beyond

- Centralized Lentiviral vector Production from our cGMP facility in Navi Mumbai.
- At scale, regionally decentralized CAR-T cell therapy production hubs proximal to hospitals and decentralized CAR-T manufacturing.
- Logistics, Patient-Enrollment support, and training/observership programs/workshops for hospitals and other treatment centres.

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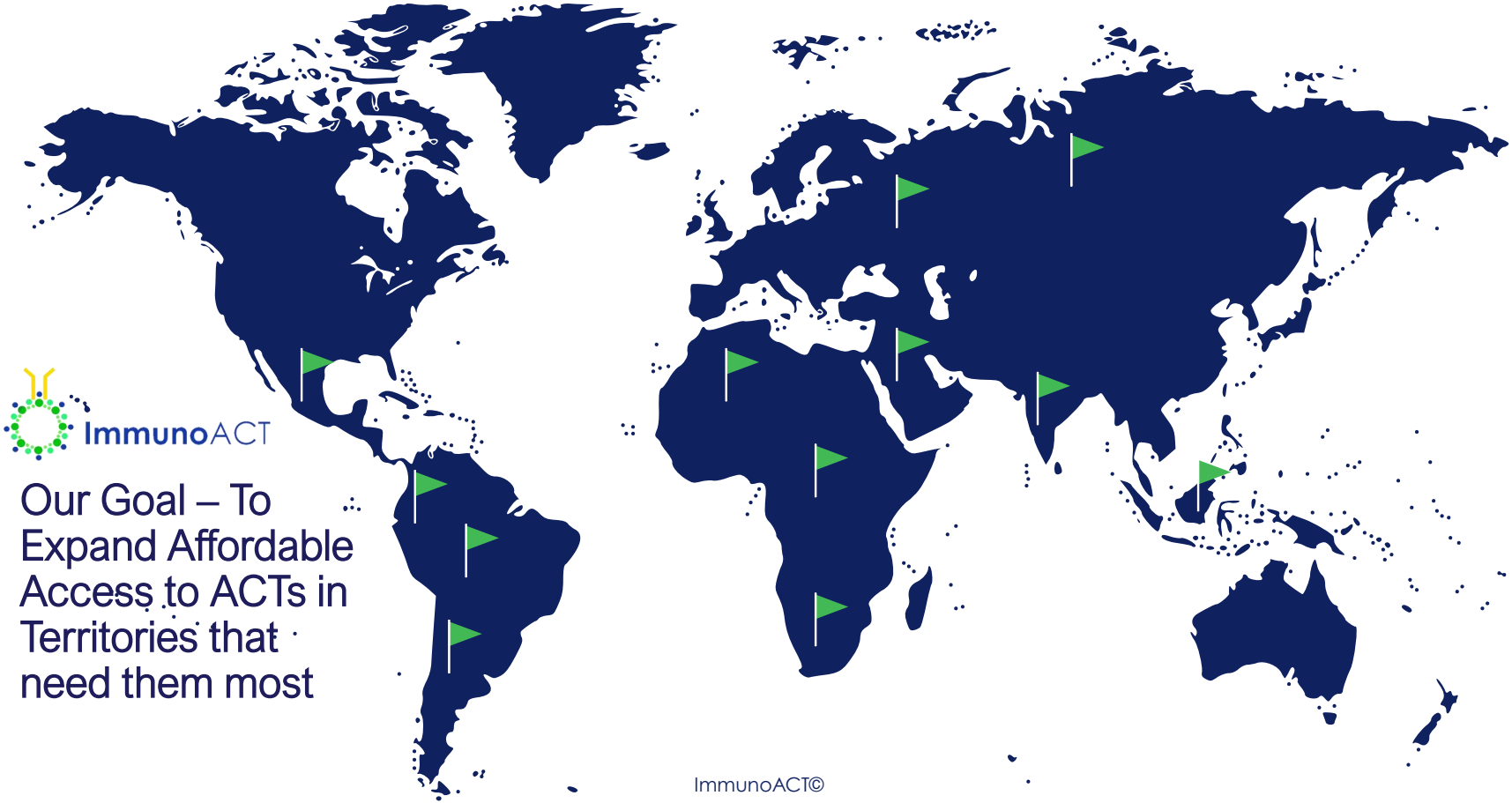
a norstella company



ImmunoACT

Our Goal – To Expand Affordable Access to ACTs in Territories that need them most

Acknowledgements

CAR-T cell technology development

1. Ankesh Jaiswal, PhD student
2. Sweety Asija, PhD student
3. Aalia Khan, PhD student
4. Ankit Banik, PhD student
5. Ambalika, MSc-PhD

Lab alumni

1. Atharva Karulkar
2. Alka Dwivedi
3. Atish
4. Moumita Bose
5. Sarbari Ghosh

Funding agencies:

CART: Tata Trust, WRCB, Tata Center, IIT Bombay, BIRAC, ICMR CSIR, DST

Collaborators & partners

TMC, Mumbai

Dr. Gaurav Narula, Dr. Hasmukh Jain, Dr Shripad Banavali, Dr Chetan Dhamne, Dr Navin Khatry, Dr Minal Poojary & their teams

NIH/NCI, USA

Dr. Terry Fry, Dr. Steven Highfill, Dr Nirali Shah

U.Penn

Dr. Carl June, Dr Avery Posey

MD Anderson Cancer Center

Dr. Sattva Neelapu & Dr Nitin Jain

ImmunoACT team

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Thank You