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Accelerating Access to Cell & Gene
Therapies in India

Bringing Cell & Gene therapy to India : Manufacturing and Development Challenges

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Executive Leadership

Kiran Mazumdar Shaw



Executive Chairperson, Biocon

Siddhartha Mukherjee
M.D, DPhil



Cancer Physician, Columbia Univ,
Scientific Co-founder, Vor Biopharma

Kush M Parmar
M.D, Ph.D.



Managing Partner, 5AM Ventures

Arun Anand
M.D.



Translational Medicine Professional,
Business leader (MGH/Harvard,
Biocon & Dr. Reddy's)

Chief Operating Officer

Founders

Cross-border leadership team with strategic relationships spanning US biotech Industry, US academic medical centers, and Indian biotech.

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Immuneel's Mission

Dramatically increase the access of transformational cell-based immunotherapies for cancer patients in India & the region.

Scientific Advisory Board

Carl H June, MD



Barbara and Edward Netter
Professor in Cancer Gene
Therapy, University of
Pennsylvania

Bruce Levine, PhD



Richard W. Vague Professor
in Immunotherapy,
University of Pennsylvania

Noopur Raje, MD



Director, Center for Multiple
Myeloma, Massachusetts
General Hospital

Vijay Chiruvolu, Ph.D., MBA



Chief Technical Officer, Instil
Bio, ex-Head of
Manufacturing, Kite

Bala S Manian, Ph.D



Chief Executive Officer &
Founder, ReaMetrix Inc.

Scientific Advisory Board includes cell and gene therapy inventors and leaders

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Immuneel aims to solve bottlenecks of cellular therapies in India & globally

| | Current Needs | Immuneel |
|---------------------|---|---|
| Availability | <ul style="list-style-type: none">▶ CAR-T therapies currently unavailable in India | <ul style="list-style-type: none">▶ Will commercialize first Indian CAR-T with world-class quality |
| Cost | <ul style="list-style-type: none">▶ CAR-T costs highly prohibitive even in US/EU | <ul style="list-style-type: none">▶ Substantially reduce costs by production in India |
| Capabilities | <ul style="list-style-type: none">▶ No current capabilities for cell manufacturing in India | <ul style="list-style-type: none">▶ Building scalable ecosystem for cGMP manufacturing and delivery of cell therapies |

cGMP: Current Good Manufacturing Practice

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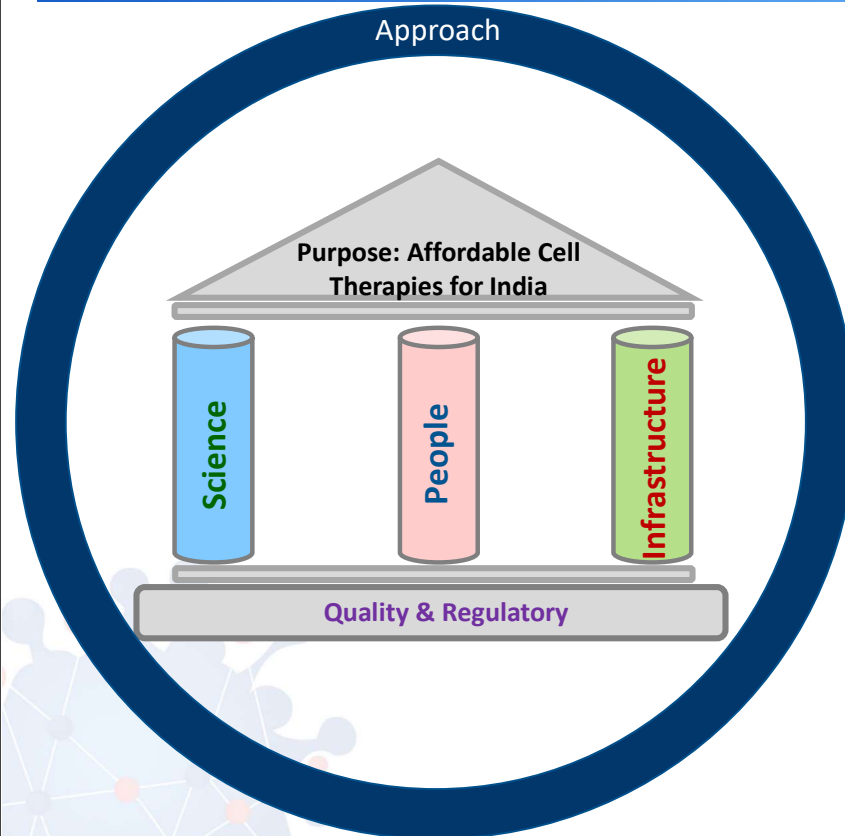


Immuneel is an Indian Start-up

Our focus and Approach is Purpose Driven



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Purpose: Dramatically increase the access of transformational immunotherapies for cancer patients in India.

Immuneel is committed to:

- Address the unmet medical need in India for transformative next-generation therapies.
- Disrupt current status quo and dramatically improve cancer patient survivability using cell & gene therapy
- Focused on starting this transformation by bringing India's first CAR-T cell therapy to India at a fraction of costs of currently approved therapies in US/EU.
- Go beyond CAR-Ts, into other forms of engineered cell therapies and gene therapies, including allogeneic therapies
- Stay focused on bringing next-gen but affordable and disruptive therapies

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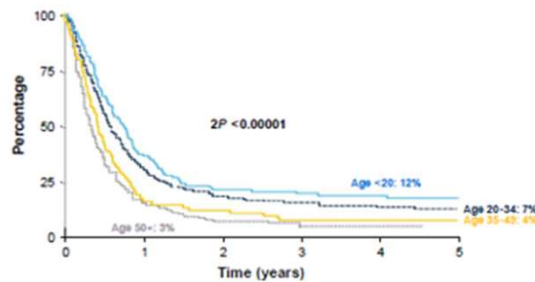
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Poor Prognosis of Relapsed ALL & B- NHL : CAR-T 'bringing hope where none existed'



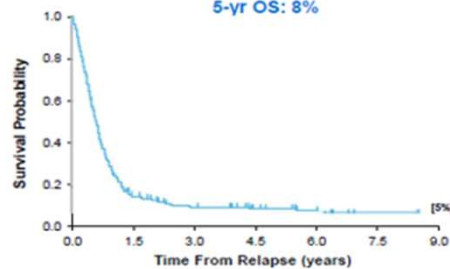
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MRC UKALL2/ECOG2993 Study (n = 609)
Outcome of patients after 1st relapse
5-yr OS: 7%



Flelding A, et al. Blood. 2007;109(3):944-950.

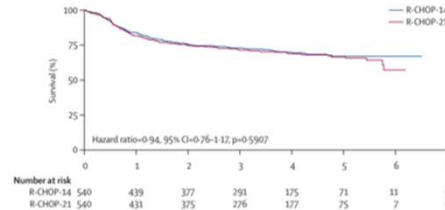
LALA-94 Study (n = 421)
Outcome of patients after 1st relapse
2-yr OS: 11%
5-yr OS: 8%



Tavemier E, et al. Leukemia. 2007;21:1907-1914.

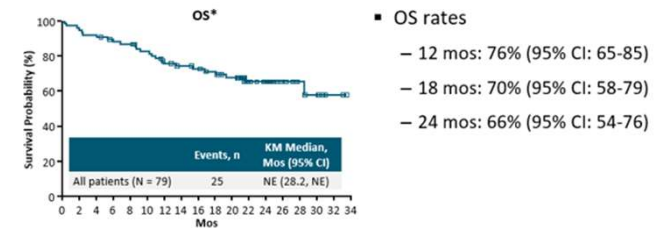
R-CHOP-21/14 Cures Up to Two-Thirds of "All Comers" With DLBCL: OS

R-CHOP 14/21 "Gold" Standard



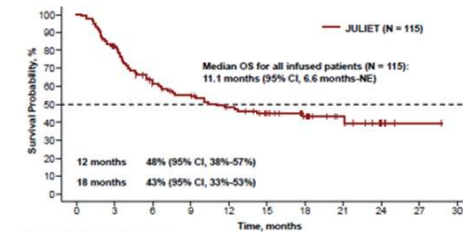
Cunningham D, et al. Lancet. 2013;381:1817-1826.

ELIANA Updated Analysis: OS



Grupp ASH 2018, Abstr 895.

JULIET: Median Overall Survival
Median OS not reached (95% CI, 21 months-NE) in patients in CR



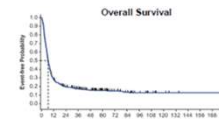
Number of patients still at risk

| Time, months | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 |
|--------------|-----|----|----|----|----|----|----|----|----|----|----|
| JULIET | 115 | 91 | 64 | 44 | 30 | 24 | 12 | 0 | 1 | | |

➤ No patients proceeded to allogeneic SCT or auto-SCT while in remission

SCHOLAR-1
(Retrospective Non-Hodgkin Lymphoma Research)

- SCHOLAR-1, a retrospective, international, patient-level, multi-institution study and the largest reported analysis of outcomes in patients with refractory large B-cell lymphoma, demonstrated that these patients have a very poor prognosis^{1,3}
- N = 636 (post-rituximab era, 2000-2017)
- ORR = 26%
- CR rate = 7%
- Median OS = 6.3 months
- These results provided a benchmark for evaluation of new approaches



CR, complete response; ORR, objective response rate; OS, overall survival.
Relapse-free survival defined as progressive disease or best response to any line of chemotherapy, stable disease as best response to a 4 cycles of first-line therapy or 2 cycles of later-line therapy, or response + 12 months (385 patients).
Response to therapy was determined by the 1999 International Working Group response criteria.

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CAR-Ts have transformed outcomes in Haem Malignancies

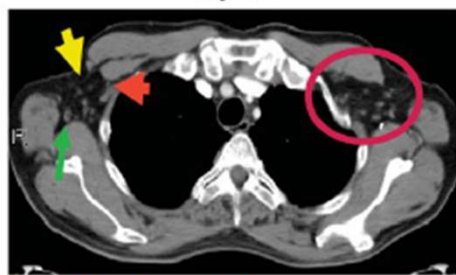
Acute Lymphoblastic Leukemia (ALL)

3m ORR Tripled, 12m OS Doubled

Baseline



Day 83

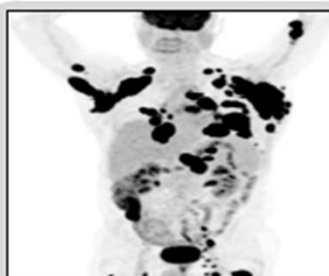


Source: Milone, June et al 2011

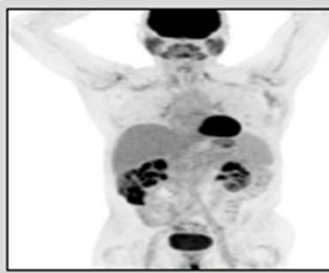
Non-Hodgkin lymphoma (NHL)

12m OS TRIPILED <30 -> 60+%

Baseline



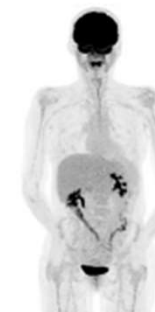
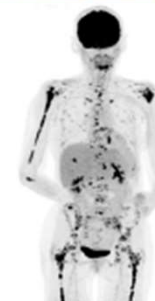
Day 90



Source: Gilead

Multiple Myeloma (MM)

3m ORR TRIPILED <20% -> 80+%



Source: National Cancer Institute

Cell Therapies, like CAR-Ts, are likely to be key in future of Cancer therapy

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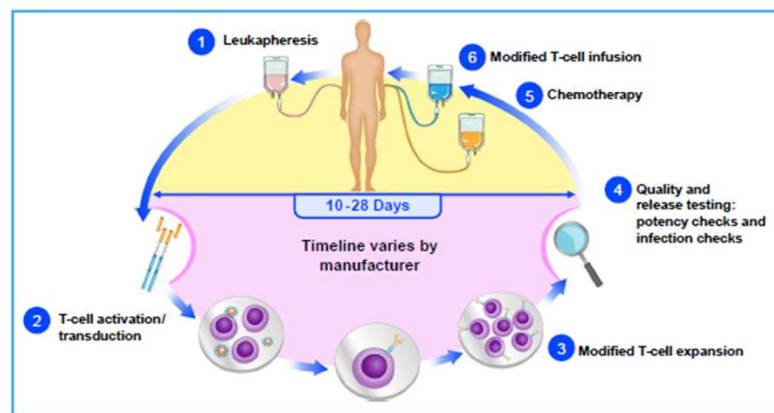


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Overview of CAR T Therapy



YESCARTA
(axicabtagene ciloleucel)
Indicated in diffuse large B-cell lymphoma (DLBCL)

TECARTUS
(brexucabtagene autoleucel)
Indicated in mantle cell lymphoma (MCL)

Abecma
(idecabtagene vicleucel)



KYMRIA
(tisagenlecleucel)
Indicated in acute lymphoblastic leukemia (ALL) in 2017, and DLBCL in 2018

Breyanzi
(lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

| Disease | Annual Incidence (ICMR) | | Relapse / Refractory |
|---------|-------------------------|--------|-----------------------------|
| | Paediatric | Adult | |
| B -ALL | 19,350 | 2,150 | 15% Paediatric 70% Adult |
| B- NHL | - | 41,600 | 30% pts |

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Pipeline

Near term pipeline

| Programs | Therapeutic Area | Target | Preclinical | Clinical | Approved |
|------------|---------------------|-------------|-------------|----------|----------|
| IMN – 003A | B Cell Malignancies | CD 19 | | | |
| IMN – 001 | Haem/Onc | Undisclosed | | | |
| IMN – 002 | Haem/Onc | Undisclosed | | | |

Mid to long term pipeline



Blood Cancers to Solid tumors

Immuneel is currently focused on treatments for leukemias and lymphomas. It aims to develop cell therapies for other diseases like solid tumours as well



Autologous to Allogeneic

Current treatments like CAR-T are autologous—a personalized treatment, made by weaponizing the patient's own immune cells. In the future, the aim is to make available a non-personalized, off-the-shelf version of cell and gene medicines. Called allogeneic, they will use human immune cells, but not the patient's own.



Beyond CAR-T

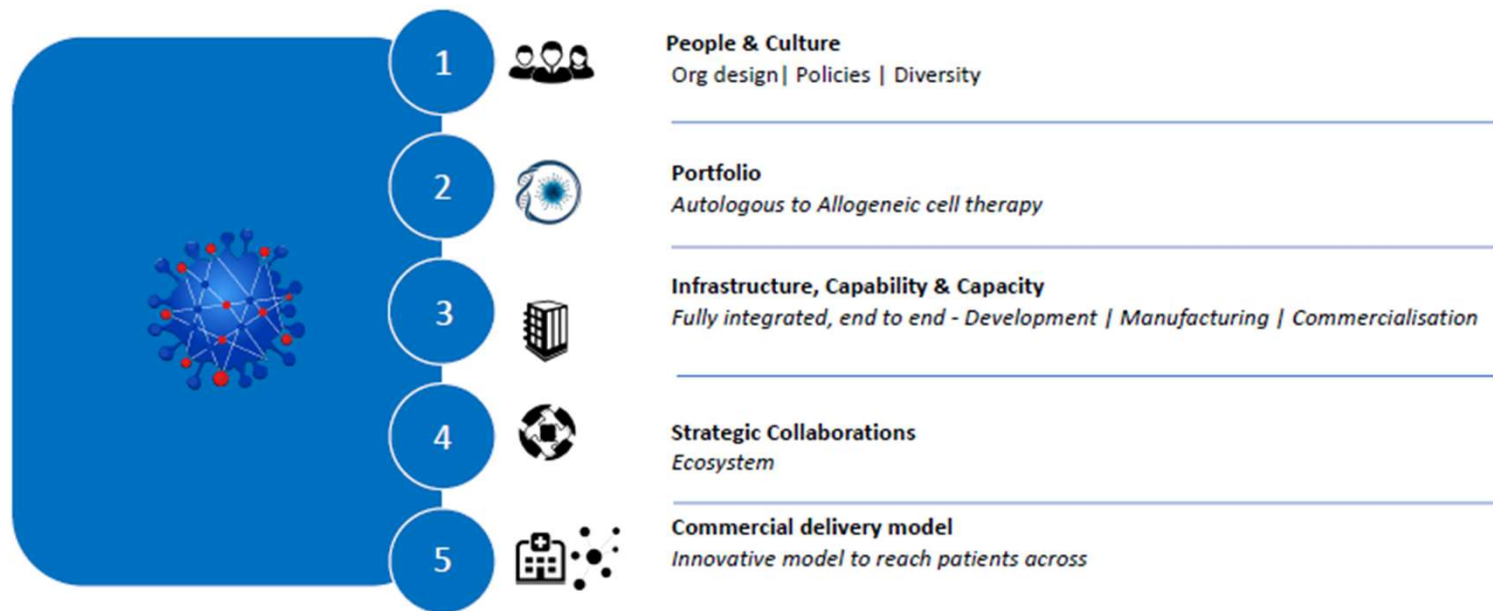
While CAR-T can revolutionize cancer treatment today, it also opens the door to other cell and gene therapies, which harness the body's cells to combat disease. Innovation will aim to improve every aspect of the treatment: the cells targeted, the modifications we design and the methods of delivering curative cells.

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We are building access to Cell therapy for the region



Immuneel will deliver scalable cell therapy benchmarked to global quality at disruptive costs

Only company in India that has razor sharp focus on affordable Cell & Gene Therapy





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Access to State of the Art Patient Infrastructure



First hospital collaborator - Mazumdar Shaw Medical Center at Narayana Health City

- Immuneel's registered "Hub" is at Narayana Hrudyalaya Health City in Bangalore with the cGMP manufacturing facility at the Mazumdar Shaw Medical Center hospital (first hospital collaboration).
- This core location in close proximity to the Bone Marrow Transplant Unit (>1000 patients, 150-200/yr) and Haematology Oncology unit of the Center, empowers Immuneel with extensive clinical & BMT experience and also bring us closer to the patients community.

Unique location giving a better access to Clinical Trial & Patient Care



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Immuneel's Facility



Quality Control Labs



R&D Labs



Manufacturing Suites





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Development & Manufacturing



- Strategically located in a hospital with access to high quality tertiary care oncology clinical infrastructure
- India's first Integrated Cell Therapy Development and Manufacturing Facility spread over 12,000 sft at Narayana Hrudayalaya Health City, Bangalore
- Office, discovery & process development labs

- State of art facility for cell & gene therapies
- Multi-process, multi-suites, multi-product, multi-patient facility for CT & commercialization
- Compliant to Indian GTP & Global cGMP guidelines for ATMPs (EMA) and FDA standards

- Both Integrated & Semi-integrated, closed cell manufacturing processes
- A digital paper-less ecosystem, safe & sustainable
- Center of Excellence for cell manufacturing
- Reproducibility. Scalability. Efficiency
- Asset & Process innovation focus

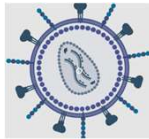
The Future of Care

Investing in developing technologies and capabilities to deliver cell therapies at scale, cost effectively with consistent and high quality

Manufacturing & Developmental challenges



Infrastructure – cGMP



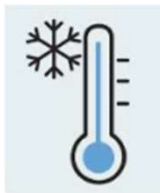
LV Constructs – GMP, I-H / CDMO



QC release assays



Chain of ID, custody, condition – personalised product



Logistics – cold chain



Delivery model :
Centralised/Decentralised / Mixed

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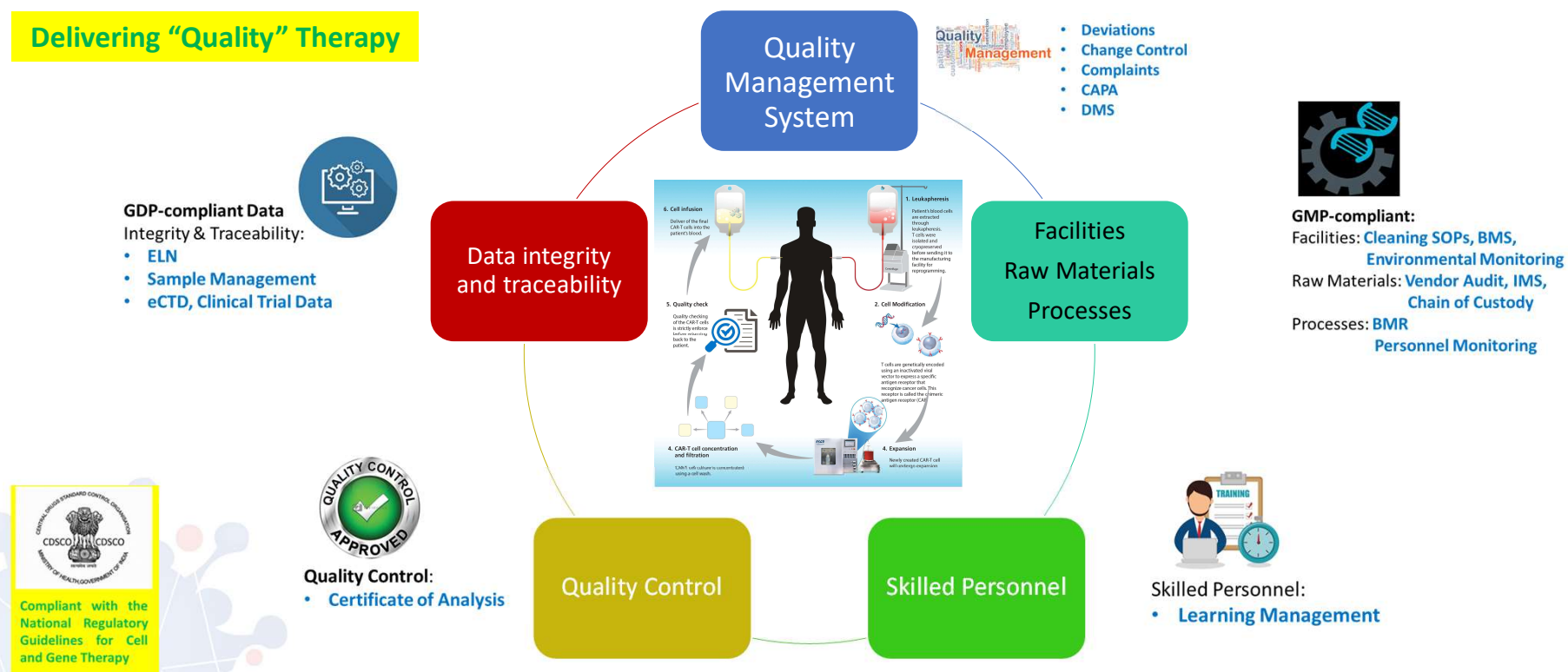




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Immuneel Quality Framework is based on National Guidelines for GTP

Delivering "Quality" Therapy



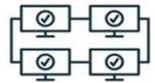
GXP Compliant Digification of Facility, Processes, Training, Data, Sample and Quality Management Systems

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Manufacturing & developmental challenges



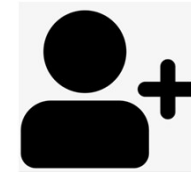
Clinical Development – Roadmap to IND filing ; Regulatory plan



Protocol – patient cohort, indication, numbers , hypothesis

PROTOCOL

Adaptive trial design / Patient safety



Site selection criteria

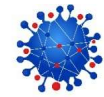
Training & Education



Covid preparedness

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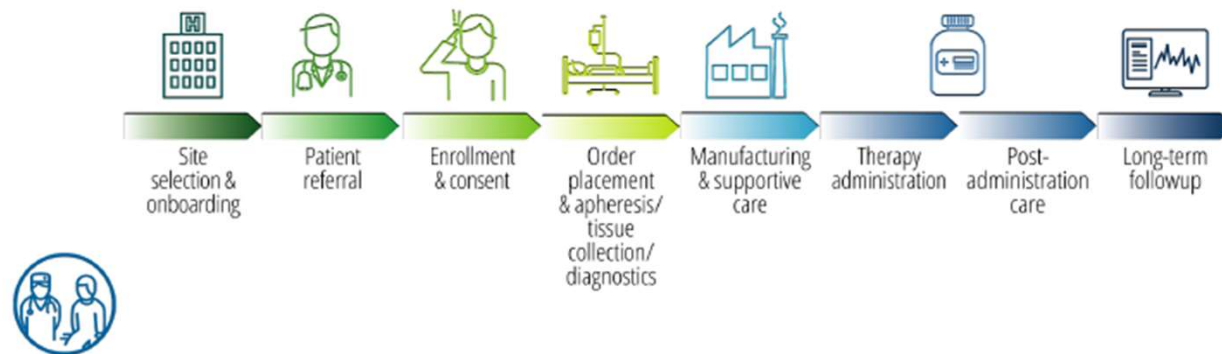




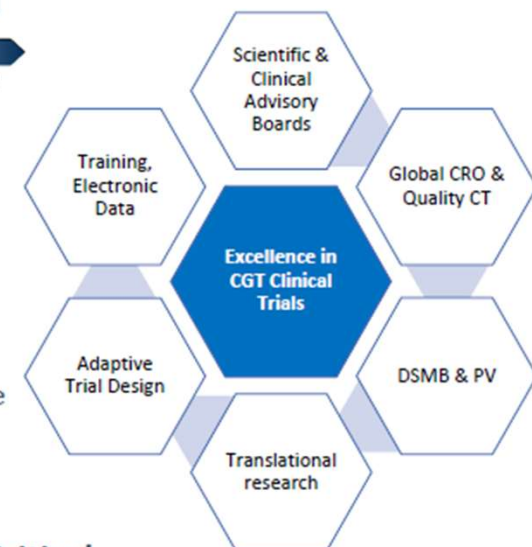
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Building Clinical Trials for Cell Therapies: Leveraging global experience

Patient centric value chain



- Experienced BMT Unit, including clinical trials
- Fully leveraged experience of SAB in Cell Therapy -> training of investigators & staff
- Strategic Clinical trial execution partnership with a global CRO with global CGT trial experience
- Adaptive Trial Design – catering to lean design with pre-specific endpoints
- Regulatory interactions to build in pathway to MAA
- Electronic database, Safety monitoring, Translational endpoints

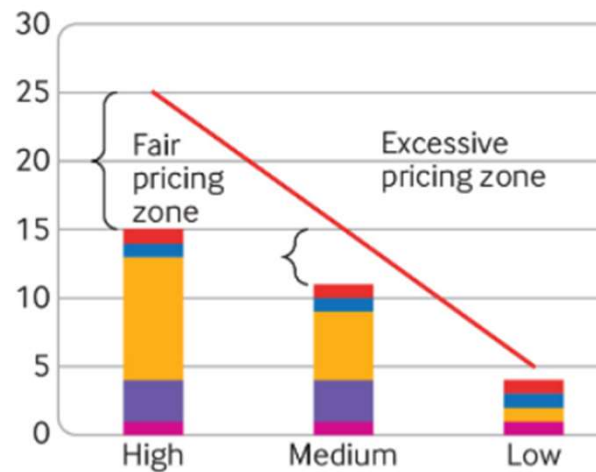


Clinical Trial is expensive and High Quality of Trial is Critical

MAA: Marketing authorisation application CGT: Cell & Gene Therapy DSMB: Data and Safety monitoring board PV: Pharmacovigilance

Manufacturing & developmental challenges

Affordability – ‘mind the gap’



Optimise on the ‘costs’

- Consumables
- Labour
- Overheads
- Transport

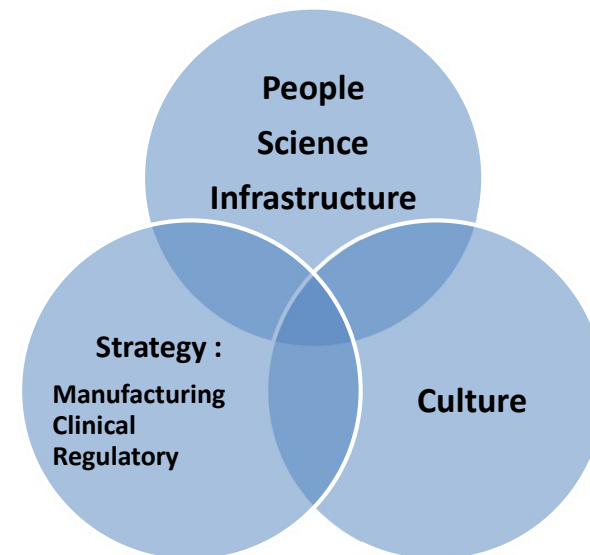
Key to sustainable and more affordable cell therapy is allogeneic therapy that is off –the –shelf, multi-patient and /or universal



**Mission with a vision :
Team Work**

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Clinical Trial IMN-003A

Immuneel will do a phase 2 bridging study in India to obtain commercial approval in India:

Manufacturing at Immuneel for cell therapy product

Clinical exposure with product manufactured at Immuneel for patients in India

Same manufacturing process & same vector as used in ARI-0001



Summary



1

Focused Executive Leadership supported by Stellar SAB and focused core team committed to bringing transformational cancer therapies to India.

2

Purpose – built 12,000 sq ft integrated cell therapy development & manufacturing facility, with close proximity to a BMT unit.

3

Near term clinical delivery through a broad autologous CAR-T pipeline focussed on haem-onc through in-licensing and in-house development

4

Investments made in sustainable and scalable manufacturing platforms to cater to commercialization of cell therapies in India + region.

5

Public & Private collaborations to build an ecosystem to deliver high quality & affordable cell therapy.

6

Potential to expand beyond India to other regional geographic locations transforming many more patients' lives.



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Immuneel is bringing **breakthrough** cancer treatment to India. Affordably.

Cell, gene and immunotherapy are at the frontier of cancer treatment, offering real hope to millions. In the few countries, where cell therapies are available, these are very expensive, and access is limited.

Immuneel, led by a group of healthcare visionaries across US & India, is making cell therapies affordable and accessible in India, for India.

