July, 2019

“Discover in India” – Strengthening the innovation ecosystem for Pharmaceuticals

IPA
Innovation, Quality and Global Reach

WHY INNOVATION IS CRITICAL FOR INDIAN HEALTHCARE SYSTEM

Starting from a nascent position in 1960s, Indian pharmaceuticals industry has emerged as the pharmacy of the world. The Indian industry has played a key role in driving better health outcomes across the world through its affordable and high-quality generics drugs. Increased accessibility to affordable drugs has helped reduce disease burden in the country by 36 percent[1] between 1990 and 2016 and has also brought down treatment cost for several life-threatening diseases to <5% of its original cost[2]. India has also enabled access globally by supplying ~60% of global vaccine supply[3] and ensuring access to AIDS treatment to 37% of patients in Africa in 2009 compared to just 2% in 2003 [4]. The industry has also contributed significantly to India's economy by providing employment to 2.7 Mn people[5] and generating USD 10 Bn in trade surplus every year[6].

Going forward, India now needs to expand its presence in the innovation space which continues to account for 2/3rd of the global pharmaceutical opportunity. Building this presence can generate substantial health benefit for India by enabling development of drugs for India-specific ailments which do not get adequate attention globally (e.g., drug-resistant infections like NDM-1; oral cavity cancer, where India accounts for ~30% of diseases burden[7]). It will also enhance industry's contribution to India's economy (additional USD 10-12 Bn in exports every year) and create large pool of white-collar jobs to enhance India's differentiation vs. other developing economies. It is however critical for India to move fast on this innovation journey as it currently runs the risk of being left-behind by countries such as China, which have been progressing rapidly to capture this opportunity (e.g. China has scaled-up its NME pipeline by 3X in last 3 years while the VC funding for pharma innovation has growth by 8X to ~USD 17 billion in the same period).

India has several strengths (e.g. strong local industry, deep technical capabilities) which it can build-off to address this competition and emerge as a successful a hub for pharma innovation. Concerted actions by industry and government can address some of the challenges in the ecosystem (e.g. regulatory bottlenecks) which are impeding India's ability to unleash its innovation potential. These initiatives can help India evolve from the position of "Make in India" to the vision of "Make and Discover in India." The aim is to create a vibrant enabling innovation ecosystem to deliver 3-5 NMEs and 8-10 incremental innovation products every year by 2030 and realise significant health and economic benefits for the country.

[1] Measured as Disability Adjusted Life Years (DALYs) after adjusting for changes in population age structure

[2] Includes cost for Hepatitis-C and Chronic Myeloid Leukaemia: Access to Costly New Hepatitis C Drugs: Medicine, Money, and Advocacy, Oxford Journals, Vol 61, Issue 12; Changing cost of care for chronic myeloid leukaemia, PMC, October 2015

[3] Press Information Bureau: "Affordable Efficacious Medicines – All Roads Leads to India", 2013 report by IDMA; Brand india pharma.in

[4] Pharmaceuticals: India's generics flow to Africa, African Business Magazine, 19 January 2012

[5] Includes direct and indirect employment: Indian life sciences: Vision 2030, FICCI Jun 2015, Growth est. by IHS Market

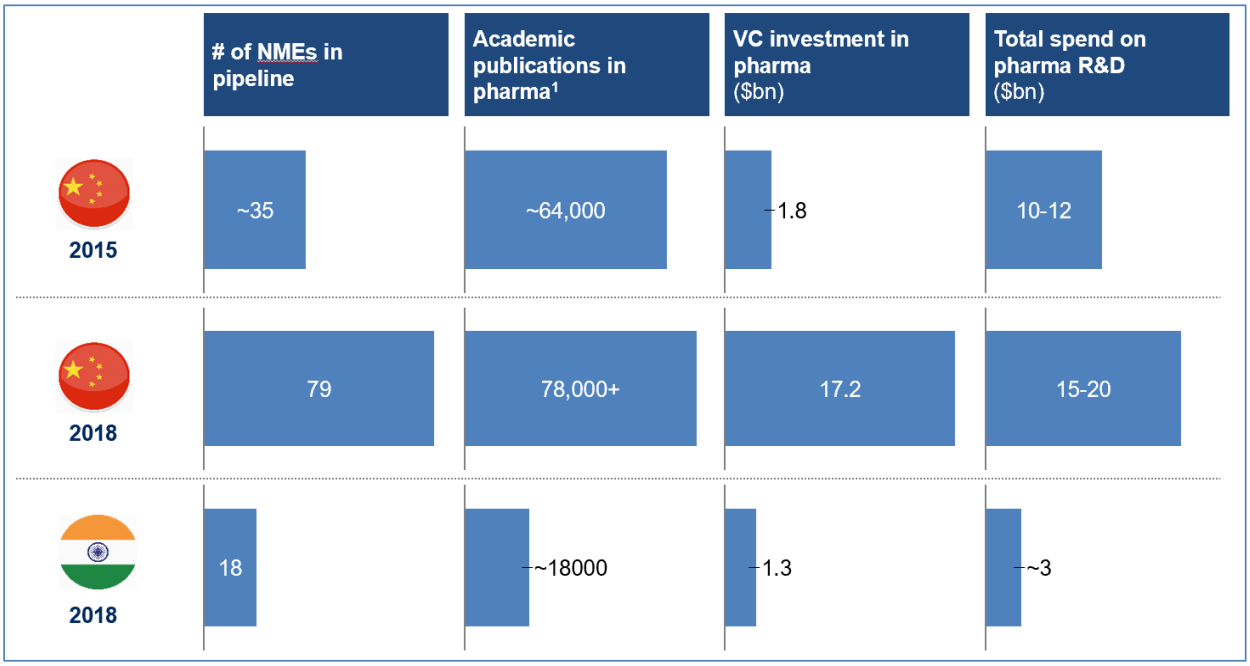
[6] EXIM Data Bank, Department of Comm, PHARMEXCIL, IDMA report - "Journey towards Pharma 2020 & beyond"

8 Cancerindia.org

LEARNINGS FROM BUILDING SUCCESSFUL INNOVATION ECOCYSTEM

Innovation landscape in Pharma has traditionally been concentrated in few clusters in developed markets (e.g., US). The landscape is now changing rapidly with few countries such as China emerging rapidly in this space.

China's rapid progress in the innovation vs. India



1 Includes all publications under Biochemistry, genetics and molecular biology

SOURCE: Pharmaprojects, World Bank data, SJR country Rank, Press search ,Team analysis

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Seven common themes emerge from the journey of these innovation hubs. China's journey across these 7 elements has been detailed out below. *Exhibit 1* captures details about these common themes for China and Israel.

- **Streamlined regulatory landscape** – China undertook a holistic transformation of its regulatory framework over 3 years to rapidly improve speed of approvals (from 35 to 21 months and 6 months for priority approvals[8]). Several initiatives were taken to achieve this including systematically augmenting regulator capacity and capability (e.g. establishing Centre of Regulatory Excellence in universities), harmonising guidelines with ICH standards, easing process for clinical trial approvals, strengthening IP protection by granting fair timelines, shifting burden of proof from reviewer to sponsor and enhancing transparency and collaboration through the process. Exhibit 2 captures the details of these initiatives.

- **Adequate rewards for innovation** – China enhanced attractiveness of its local market for innovative drugs by reforming pricing and reimbursement policies to ensure swift inclusion of innovative products in reimbursement list (39 novel products included in third round of National Negotiation Drug list in 2017) and collaborating with MNCs (e.g. Roche on oncology) to enable broader access and adoption of innovative products.

[8] Impact of reforms, *An overview of major reforms in China's regulatory environment*, Bill Wang, Alistair Davidson

- **Strong funding support** – China drove sharp increase in funding for pharma innovation (~4X growth over 5 years to ~USD 15 bn+ in 2017 with government spend growing by ~30% y-o-y)[9]. Several actions were taken by government to drive this, including (1) Direct funding support for basic research (~USD 4 Bn in 2016[10]) with strong linkage to quality of research, (2) Easing availability of risk-capital from VCs through structured engagement and providing seed capital (e.g., 50% of capital in local currency VC is by government)[14], (3) Financial incentives to industry through tax rebates and debt funding and (4) opening by IPO markets for start-ups by easing listing regulations in Hong Kong.

- **Strong talent pool** – China embarked on a "reform and open door" policy- global scholars were invited to come back under the "Thousand Talents Plan" that offered generous research grants and conferred social pride – this led to 250,000+[11] Chinese educated in US returning ("sea turtles"). China further enhanced attractiveness of research career path by increasing compensation to accomplished researchers (e.g., up to USD 85,000) and rewarding young researchers through grants (Up to USD 250,000).

- **High quality research by anchor institutes** – China launched "project 985" to build Ivy league equivalent institutes ("C9") in China and established multiple universities (e.g., Tsinghua, Peking) in Global top 100. Initiatives taken to enable this include creating five specialized groups of institutes to drive focused research, significantly boosting funding for these universities to western university levels, and improving faculty and infrastructure.

- **Innovation clusters offering high quality infrastructure** – China created large biotech parks/ clusters of innovation (e.g., Chengdu, Taizhou). These clusters enabled co-location of various stakeholders (e.g., academia, industry, VC, regulator), provided 'plug and play' infrastructure (e.g., built out labs, biomedical waste disposal facilities) and financial incentives that resulted in highest number of incubators (7,500+) for pharma innovations.[12]

- **Outreach and promotion** – China actively focused on promoting its progressive innovation environment in global events (e.g., World Economic Forum) and initiated inter-government collaboration (e.g., US-China Biopharma Innovation and investment).

ASSESSMENT OF CURRENT INNOVATION ECOSYSTEM IN INDIA

While India has witnessed some early successes with 5+ NME launches already and 15+ assets in pipeline, overall scale of innovation continues to significantly lag other markets, driven by gaps across all elements of innovation ecosystem. This includes

- **Regulatory landscape** – While some improvements have been made over last few years (e.g., new clinical trial guidelines), overall regulatory framework continues to have several gaps. Exhibit 2 details out these challenges across – (a) Complexity in approval process (especially for biologics and toxicity studies), (b) Subjectivity in reviews driven by lack of adequate guidelines and variability in expert inputs, (c) Long process due to lack of defined timelines, (d) Challenges in capacity and capability of regulatory body, (e) Absence of accelerated approval pathways, and (f) Gaps in transparency and collaboration with industry. These gaps lead to long approval timeline in India and significantly impedes pace of

[9] Research and Markets, China Biocentury report, Natural Science Foundation of China; National Science and Technology Major Project; China Statistical Yearbook on Science and Technology

[10] The NSFC programs, *China's approach to attract and nurture young biomedical researchers*, Cong Cao

[11] Press search – South China morning post

[12] Total incubators, and not restricted to pharma – basis Chinadaliy

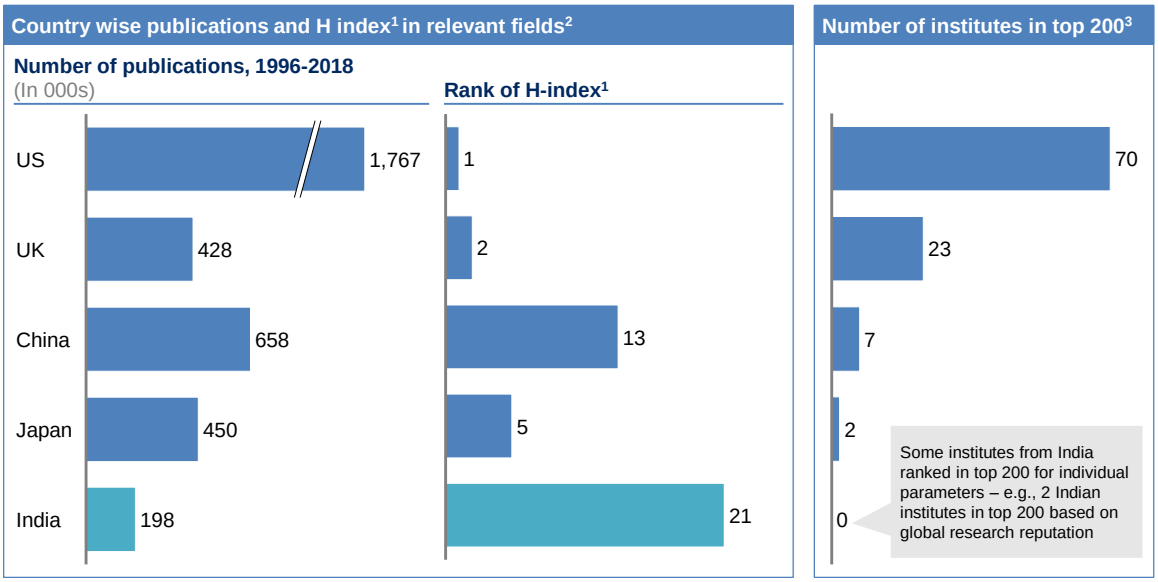
innovation in the country (e.g., average time for clinical trial approval was 400+ days for biologics and 250+ days for NCEs V/s 30 days in USFDA13). Similar challenges also exist for patent grant (timelines of up to 8 years compared ~2 years in US and 2.5-4 years in China).

- **Funding support** – Level of funding for pharma innovation in India continues to be significantly lower than other markets (estimated to ~USD 3 Bn in 2018 vs. ~USD 15+ Bn in China and ~USD 100+ Bn in US). Government spend in India is considerably lower (~25% of total R&D spend in India vs. 35%-60% in other markets[14]) with opportunity to improve effectiveness of the existing spend and shift it towards early-stage research. Spend from industry is also lower due to by highly risky nature of investment and absence/ roll-back of incentives. The VC ecosystem in the country has also not developed adequately due to lack of historical track-record for innovation and lack of conducive policies (e.g., permissions for change in majority stake due to VC exit in an asset with government stake). Details on these challenges are captured in *Exhibit 3*.

- **Reward for innovation** – Competitive pricing levels in Indian market and lack of any central reimbursement programs (e.g., NRDL in China) that can facilitate uptake limits the opportunity for innovative products in the country. This has further constrained the level of focus on innovative portfolio both by local as well as MNC players for India.

- **Quality of research in academia and industry collaboration** – Quality of local research in India also continues to lag global leaders driven by multiple challenges. Multiple challenges in the performance management approach, supporting infrastructure and structured collaboration with industry are driving these challenges as detailed in Exhibit 4.

Quality of academic research in India vs peer countries



1 H-index (Hirsch index) is a metric to measure the productivity and citation impact of publications for a particular scholar
2 Includes research in fields of Biochemistry, genetics and molecular biology from 1996 – 2018
3 Ranking based on ranking across 13 factors like Global research reputation alone; publications, impact of citations etc.
SOURCE: Scimago journal and country ranking; USNews global university rankings

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13 Average timelines for India calculated basis 9 products from 2 companies; US timelines basis median CDER approval timelines for standard NDAs and BLAs from FDA

14 New Engalnd Journal of medicine; Evaluate (2013)

- **Quality of local talent** – India continues to lack the high-quality talent required to drive innovation effectively in the country. Quality of local talent is impacted by curriculum and lack of adequate industry exposure in universities. Lack of adequate policies also limits India's ability to attract back high-quality global Indian talent (e.g., VAJRA is a 1-3 months visiting program as opposed to encouraging innovators to move back permanently).

- **Limited at-scale innovation hubs with best-in-class infrastructure** – While few clusters exist in India (e.g., Genome valley), they have been unable to get the required scale due to lack of holistic support (e.g., co-location of other stakeholders) and absence of the full innovation ecosystem in the country (e.g., funding support).

PATH FORWARD FOR ENABLING THE VISION OF "DISCOVER IN INDIA"

Although these challenges exist, several enablers including a strong local industry and depth of technical capabilities can help India work towards the vision of "Discover in India". These enablers can help India in building a strong ecosystem for healthcare innovation delivering 3-5 NMEs and 8-10 incremental innovation products annually from 2030. Achieving this vision will not only benefit India maintain its global relevance but will also drive several health and economic benefits for the country as stated earlier. Realising this vision will require concerted actions across all stakeholders and the Government can play a critical role in catalysing this journey through two sets of initiatives.

Create enabling environment for industry to drive innovation in short term

1. **Simplify regulatory framework to aid innovation** – Government can build off the positive momentum of recent reforms and undertake a holistic transformation to create an enabling regulatory environment for innovation. In addition to implementation of Mar'19 clinical trial guidelines, five key initiatives that can be undertaken for this journey are:

    a. **Reduce complexity in the approval process -** Three specific initiatives that government can explore as part of this include – (i) Reduce number of overlapping approvals for biologics e.g., empowering IBSC to approve start of research (V/s IBSC and RCGM approval), streamline approval for toxicity data that currently involves IBSC, RCGM and DCG(I), (ii) Enable faster approval for large animal studies by empowering IAEC without additional approval from CPCSEA (which can conduct periodic audits to ensure quality), and (iii) Establish accelerated and prioritized pathway for innovative products (e.g., dedicated CMC review committee in DCGI).

    b. **Strengthen consistency and quality of reviews:** Few initiatives that Government can undertake are – (i) Establish clear timelines for each stage of process (e.g., responding to queries) and performance management on those milestones to expedite approvals, (ii) Bring in consistency in working and guidance's of expert committees (e.g. participation of consistent set of experts in the process, ensure adequate quorum of 10-12 experts etc,), and (iii) Harmonize guidelines with of ICH standards.

    c. **Increase capacity and strengthen capability in regulatory bodies** – Like several other markets (e.g., PMDA in Japan, CFDA in China), India should look to significantly ramp-up capacity and capability of the regulator. India should establish dedicated capability building program (e.g., Center for regulatory excellence) in few leading universities and improve level of collaboration with international agencies to enhance experience/ exposure of Indian regulators on new drug approval.

d. **Enhance transparency and collaboration with industry** – This can be achieved by ensuring provision for pre-submission discussions (proposed in Mar'19 clinical trial reforms) is rigorously implemented and creating visibility/ transparency on the status across the approval process. India can also set up project management roles in the regulatory body to act as single-point-window for industry (in line with practices in USFDA and CFDA). India can also enhance collaboration and speed of approvals by shifting burden of proof from approver (in regulatory body) to sponsor. Initiating self-inspection of pre-clinical and clinical data by sponsors can be active steps in this direction.

e. **Ensure transparency and predictability of IP grant process** – Indian patent office can consider - (i) Establishing standard timelines for the patent grant process and performance management on those milestones to ensure adherence, and (ii) Creating visibility and transparency on status throughout the application process.

2. **Launch policies to incentivize private investment in pharma innovation** – Given the quantum of investment required (10-12% of revenues) and high risk-profile, putting in measures to encourage investments will be critical in ramping up the level of innovation. Few initiatives that the government may explore:

   a. **Incentivize industry to invest in pharma R&D** – Government may explore multiple initiatives to support the industry such as re-instating the 200% tax exemption on R&D spend, creating a preferred tax slabs for companies focusing on innovation, reducing patent box concession tax on IP to 6% (from current 10%), introducing 'Innovation' bonds to offer lower interest rate debt funding (in line with infrastructure bonds) etc. It may also consider introducing further tax exemptions on angel investments in innovation to encourage private investments in innovation start-ups. Finally, government may also consider stabilising the pricing policies to enable companies to redirect internal resources towards innovation.

   b. **Provide direct grants in a performance-linked fashion** – In line with practices in several markets (e.g., China, Israel), government may consider setting up an "innovation fund" which provides milestone linked grants (e.g., on completion of basic research, pre-clinical or clinical phases) to companies on innovation efforts. Government may also consider scaling-up funding it currently offers as part of its incubation efforts. This could be more focused (to avoid fragmentation across opportunities) and directed towards early stage discovery research to encourage breakthrough innovations.

   c. **Start encouraging VC investment through a supporting environment** – While establishing VC ecosystem will take time, it is important to start creating an enabling environment to encourage innovation. Government may consider setting up jointly-funded VC funds (e.g. building off Fund of Funds for Startups) to start investing in innovation opportunities in India. Systematic outreach efforts may be undertaken to initiate dialogue and get VC community motivated about the opportunity in India pharma market. Streamlining existing regulatory challenges (e.g., permission for change in majority stake due to VC exit in an asset with government grant) may also enable this further.

3. **Create access and enhance opportunity for innovative products in India** –Having a meaningful opportunity for the innovative products in the domestic market would be critical to encourage investment in innovation. Government may consider setting up special reimbursement mechanism for locally developed innovative drugs for priority disease areas. This may be done by government directly (e.g., similar to Russia's seven nosologies program) or in partnership with industry (e.g., China's partnership with Roche in oncology)

Structural interventions to build broader innovation ecosystem in India

In addition to the above-mentioned priorities, government may undertake four initiatives laying down the foundation of innovation ecosystem. While these initiatives will take longer time to have full impact, starting them now is critical to ensure that India is ready to effectively compete in the pharma innovation space in the longer term. These initiatives are:

1. **Enhance quality of infrastructure to support innovation** – Government may scale-up 5-6 'Innovation hubs' in the country. This would facilitate co-location of industry, academia, VCs and incubators and create a vibrant innovation ecosystem. Explicit incentives (e.g., tax exemptions) and plug and play infrastructure may be offered for companies in these parks, beside local regulatory support to enable speedy approvals/ clearances. Government may create adequate support for clinical trials by strengthening infrastructure (e.g., IT and data management systems in public hospitals) and actively encouraging clinical trial participation by government hospitals.

2. **Accelerate momentum on funding** – Government may help sustain the momentum on funding by – (a) Gradually increase public spend on R&D by additional ~USD 500 Mn focused on primary research (with emphasis on innovation focused areas such as genetics, biochemistry, molecular biology etc.) in academic institutes and grants to start-ups/ industry (can be part of recently announced National Research Foundation); (b) Encouraging alternate funding routes by ensuring rigorous implementation and further improvement of simplified listing norms proposed under Innovation Growth Platform (IGP) by SEBI.

3. **Enhance quality of research in local academia** – Government may consider undertaking a holistic transformation across four dimensions to drive a step-change in quality of research in local academic institutes including – (a) Prioritize 8-10 anchor institutes (potentially a subset of Institutes of Eminence like IIScs well as other premier science research institutes such as TIFR and ICT) which would be the focus for building world-class research capability by deployment of majority of government funds/ grants, (b) Revamp the performance management framework with increased focus on result-oriented metrics (e.g., patents granted, impact per citation) as opposed to inputs (e.g., quantity of publications), (c) Shift in curriculum to more cutting-edge topics with active encouragement for exploratory research (e.g., instituting national award for innovation) and collaboration with industry, and (d) Set up of Technology transfer office / platform to support academicians in commercializing research and getting private grants.

4. **Enhance scale of policies to attract top global research talent** – While some of the policies for attracting back global talent exists (e.g., VAJRA, Ramanujam fellowship), government can consider expanding the scale and effectiveness of these initiatives. This can be done by increasing the level of grant (e.g., China gave grants of up to ~USD 300-400k to these scholars), bestowing strong social recognition for those returning, and extending programs like VAJRA to focus on permanent relocation (rather than just part-time).

□ □ □

Building presence in the innovation space is now a critical priority for India to address the needs of the healthcare system and for it to maintain its relevance in the global pharmaceuticals industry. India has several strengths and a strong starting position to build on as it looks to evolve from its successful journey of "Make in India" to now work towards the vision of "**Made & Discover in India**". Concerted actions from industry and government can play a critical role in building the enabling environment for India to address competition from other markets (e.g. China). It can help unleash India's innovation potential and help establish itself as the innovation hub for the pharma industry globally and drive significant benefits for the country both from a health and economic standpoint.

Appendix

Exhibit 1 – Learnings from China in building a vibrant innovation ecosystem

1 Streamlined regulatory landscape	**Approval timelines reduced from 35 to 21 months** on average through ▪ **Strengthening regulatory capacity and capabilities** – Collaboration with universities to strengthen capability (e.g., Peking University & APEC Center of Excellence) – Significantly augmented (~3X) reviewer capacity ▪ **Strengthening quality of review** by harmonizing guidelines with global ICH standards and issuing 130+ guidelines, – Instituted max threshold of 6 months for **priority innovations**[1] ▪ Ease conduct of clinical trials – **Increased site availability** by removal of accreditation requirements of clinical sites – **Local clinical trial centers encouraged** to participate in MRCT[2], regional **ethics committees empowered** ▪ **Strengthening of IP protection** (e.g., 10 year for new biological & 6 year protection for new drugs) ▪ Shifting of **burden of proof from regulator to sponsor,** by initiating self inspection of clinical data ▪ Created a **transparent system** – initiated automatic approval provision for **clinical trial reviews,** institutionalized pre- and post-review communication with dedicated **project managers acting as single point of contact** across bodies for industry
2 Adequate reward for innovation	▪ **Enhanced attractiveness of local market for innovative products** (e.g., Novel oncology drugs in China 40-50% higher priced than India) to encourage research – Reforming **pricing and reimbursement policies** to ensure swift inclusion of innovative drugs in reimbursement list (~50% oncology products included in 2017 with RDPAC[3] proposing a refresh to the NRDL every 2 years) – **Collaborating with MNCs** to provide **innovative patient assistance program** to enable access and broader adoption of drugs (e.g., Roche's cancer program under which after a patient has taken the first six cycles of Herceptin, Roche donates the next eight cycles through the Cancer Foundation so that patients can complete the full course of treatment)
3 Strong funding support	Government led funding during initial years (pharma R&D spend grew by 3-4X between 2012-17 with govt. share growing by 30%) ▪ **Basic research funding** – significant funding (~USD 4bn in 2016) dispersed in a performance linked approach (e.g., peer review) – **Government grants:** initiated multiple grants for basic research (e.g., NSFC) ▪ **Startup funding** – created deep **ecosystem** for risk based financing (Healthcare VC investment **~USD 30bn** in 2017) – Structured engagement with VC (e.g., invited for screening of startups to incubate, mentorship) – Government actively provided seed capital (~50% of capital in local currency VCs is by government) ▪ **Scale up funding** – tax rebates for innovation driven companies (e.g., 75% super tax deduction on R&D expenses) – IPO market: norms for listing in Hong Kong eased; Debt funding: e.g., DNA sequencing giant BGI got $1.5 billion 10-year loan

1 Defined as Innovative drugs not approved worldwide or for HIV, cancer and rare diseases 2 Multi-regional clinical trial 3 Basis 3 oncology drugs 4 R&D Pharmaceutical Association of Companies, China 4

4 Strong talent pool	▪ China's **highest governing body** embarked on a "reform and open door" talent policy: – Increasing compensation to highly accomplished researchers (e.g., Paying up to USD 85,000) – Rewarding young researchers through grants (Up to USD 250,000) to **shift career choice** – Establishing a fair and transparent peer review system to establish research credentials ▪ Global scholars invited to join Chinese research institutes by **"Thousand talents Plan"** that offered generous research grants and confers pride- over **250,000 Chinese educated in US** returned
5 Anchor institutions	Chinese government launched an ambitious program "project 985" to build Ivy league equivalent ("C9") for China. Multiple Chinese universities (e.g., Tsinghua, Peking, Fudan, Zhejiang) entered **top 100 world ranking through this approach:** ▪ **5 specialized groups of institutes**[4] created **to drive focused research;** universities **actively collaborated** with global research groups (e.g., Tsinghua University partnered with Bill and Melinda Gates foundation) ▪ **Significantly boosted funding** with per capita funding availability coming close to western university levels ▪ Continuous focus on **strengthening faculty** (collaboration with foreign professors) and **upgrading infrastructure** (e.g., $750 million spent to construct a state-of-the-art synchrotron in Beijing)
6 Innovation clusters	▪ Creation of **large biotech parks/ clusters** of innovation (e.g., Chengdu HTIDZ, Taizhou)- highest number of incubators (7,500+) – Reduced setup cost (e.g., cheap land) with plug and play infrastructure (built out labs, biomedical waste disposal facilities) – Regulatory support (Regulators co-locate in parks to provide direct service to tenant companies)
7 Active promotion & outreach	▪ Government's outreach program for attracting MNCs helped attract investment – Highlighting China's progressive innovation environment in global events (e.g., World Economic Forum) – Government to government collaboration (e.g., US-China Biopharma Innovation and investment)

3 Source: Report prepared for US-China Economic and security review commission 4 Research Universities, Doctoral Universities, Master's Universities, Baccalaureate colleges and Associate Colleges 5

EXHIBIT 1A – Learnings from Israel's innovation ecosystem

1 Favorable regulatory environment	▪ Dedicated **Innovation Authority which has been instrumental** in setting up the innovation policy framework ▪ **Neutrality focused regulations** that create a level playing field to innovate in Israel ▪ **Policies harmonized with global regulatory standards** (US, CE, Australia etc.) with focus on **timely approvals**
2 Strong funding support	▪ **Multiple incentives for investments in innovation** from private sector – Individual investors qualifying as "angel investor" get special income tax rebates on investments done in startups – Tax income from IP is 6% vs 9% in US, incentivizing MNCs to innovate in Israel ▪ **VC investments have been core in** with VCs constituting 66% of the total USD1.2bn invested in life sciences ▪ Innovation Authority does targeted grant based investment (~USD 100mn in life-sciences) through:- – Pre-seed program: Grants are up to 85% of the approved expenses for building prototypes, registering patents etc. – Consortia R&D program: Supports the formation of consortia by providing up to 66% of the budget – Competitive R&D program: Grants from 20-50% of R&D budget; supports 1,000+ projects/year
3 Research talent	**High quality** (e.g., 4 Nobel prizes in Chemistry in past 9 years) & **high quantity (**140 engineers/ scientists per 10K employees) ▪ **Compulsory military service** that rewards studying STEM in university post the military service
4 Anchor institutes	▪ **Israel's universities are constantly rated top tier** (4 universities in top 200), with strong history of innovation and collaboration ▪ **Technology transfer offices** in universities to foster collaboration with industry v ▪ **Specific incentive programs** such as **Magneton** encouraging transfer of technological knowledge from academia to industry, via grants up to 66% of approved budget
5 6 Infrastructure & outreach	▪ Israel innovation authority **runs 24 incubator programs** which provide infrastructure, finance, and admin support ▪ Government partners to run global campaigns e.g., MIT-Israel program

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EXHIBIT 2 – Challenges in India's regulatory environment

✓ Addressed in new CT rules (Mar 2019) but needs rigorous implementation

A	**Complexity in approval process**	▪ **Multiple rounds of approvals across regulatory authorities** driving long approval timelines, e.g., – In Biologics,~15 approvals[1] required across bodies before marketing authorization; RCGM approval required to start research on biosimilar even after IBSC approval – For toxicity studies, regional approvals (IAEC) not enough to start studies in large animals (e.g., dogs)	
B	**Delays and lack of predictability**	▪ **Lack of defined timelines for regulators** to respond (partly addressed through 30 day window for default approval, but no timelines for responding to query response) ▪ **Gaps in capacity and capability in regulatory bodies** leading to delays ▪ **Lack of accelerated pathway** for innovative products (e.g., common CMC review at DCGI)	✓
C	**Subjectivity/ Lack of consistency in review**	▪ **Lack of defined guidelines** across several key areas (e.g., guidance on clinical study design); CDSCO website has 24 guidelines compared to 150+ in CFDA and 600+ in FDA ▪ **Variability in expert guidance/ queries** through the approval process (driven by factors such as lack of consistent panels)	
D	**Opportunity to enhance transparency**	▪ **Lack of pre-submission discussions** to minimize queries and help expedite approvals ▪ **Lack of visibility** (real time tracking) of applications through various stages	✓
E	**Risk-averse mindset**	▪ **Risk-averse approach** on account of full **burden of proof on approver** (rather than sponsor)	
F	**Guidelines for trials**	▪ **Ambiguity in operating guidelines for trials harmonized with ICH** (e.g., compensation guidelines, waiver of CT for approved product[2])	✓

1 Includes import license, permission for research, permission for tox study, NOC for clinical trial, test license for CT, Dossier review, CMC review across IBSC, RCGM and DCGI
2 If approved in US, UK, Japan, EU, Canada, Australia
SOURCE: Expert interviews, CDSCO, CFDA, USFDA, Team analysis

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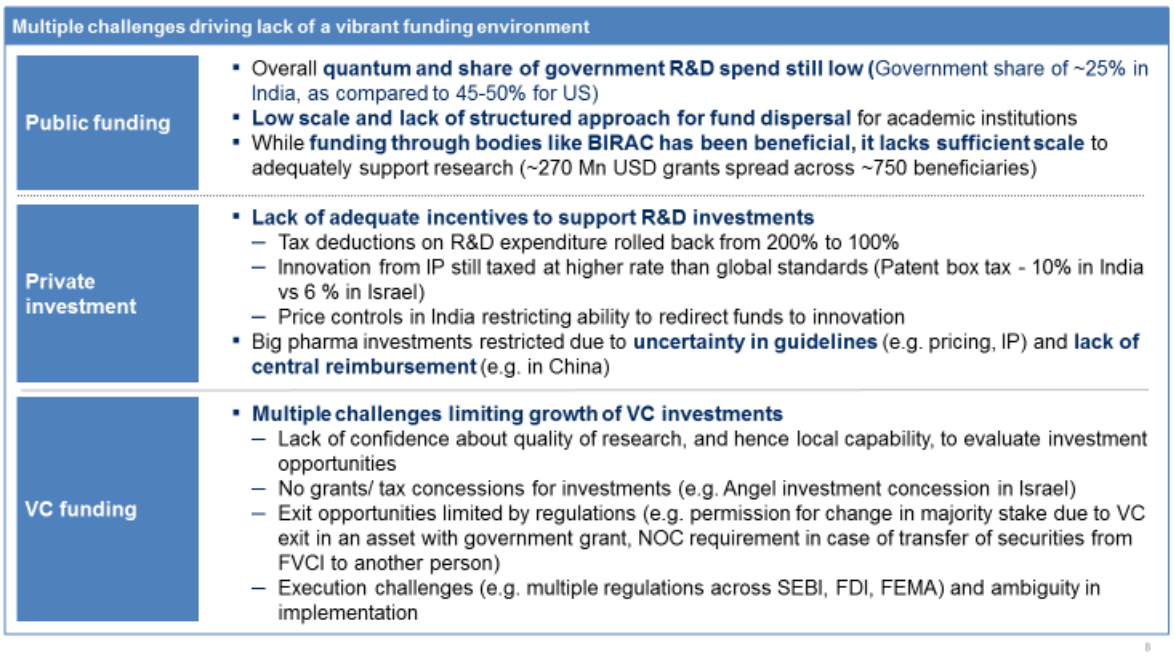
EXHIBIT 3 – Challenges in India's funding environment



Multiple challenges driving lack of a vibrant funding environment

Public funding	▪ Overall **quantum and share of government R&D spend still low** (Government share of ~25% in India, as compared to 45-50% for US) ▪ **Low scale and lack of structured approach for fund dispersal** for academic institutions ▪ While **funding through bodies like BIRAC has been beneficial, it lacks sufficient scale** to adequately support research (~270 Mn USD grants spread across ~750 beneficiaries)
Private investment	▪ **Lack of adequate incentives to support R&D investments** – Tax deductions on R&D expenditure rolled back from 200% to 100% – Innovation from IP still taxed at higher rate than global standards (Patent box tax - 10% in India vs 6 % in Israel) – Price controls in India restricting ability to redirect funds to innovation ▪ Big pharma investments restricted due to **uncertainty in guidelines** (e.g. pricing, IP) and **lack of central reimbursement** (e.g. in China)
VC funding	▪ **Multiple challenges limiting growth of VC investments** – Lack of confidence about quality of research, and hence local capability, to evaluate investment opportunities – No grants/ tax concessions for investments (e.g. Angel investment concession in Israel) – Exit opportunities limited by regulations (e.g. permission for change in majority stake due to VC exit in an asset with government grant, NOC requirement in case of transfer of securities from FVCI to another person) – Execution challenges (e.g. multiple regulations across SEBI, FDI, FEMA) and ambiguity in implementation

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EXHIBIT 4 – Challenges in Indian academia to pursue innovation

Performance evaluation framework	▪ **Performance evaluation largely on input metrics** (e.g., # of publication) rather than on quality (e.g., patent granted, ideas commercialized) ▪ **Lack of encouragement and incentive to pursue cutting edge topics** where chances of success are lower (funds typically not risked for exploratory research)
Curriculum focus	▪ **Greater focus on learning of core** pharmaceutical concepts (e.g., process chemistry, formulations) ▪ **Lack of emphasis on forward-looking areas** and limited hands-on experience relevant for the industry
Collaboration with industry	▪ **Limited instances of collaborative research** between industry and academic institutions – **Limited industry immersion programs** for faculties, who often are involved in pure academic research – **Heavy dependence of publicly funded universities on govt. aid** with little-to-no private revenue streams
Support for commercialize-tion of research	▪ **Absence of evolved tech transfer offices** across universities (for instance, TTOs in Israeli universities have expertise in life sciences specific IP management, marketing & valuation principles, help found startups and connect with industry via in-licensing and sponsored research agreements)

SOURCE: Expert interviews; Team analysis

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