nextar chempharma solutions

You invent, we make it a drug product

Paving the way to FDA?
tips and pitfalls

The Nextar start up support program

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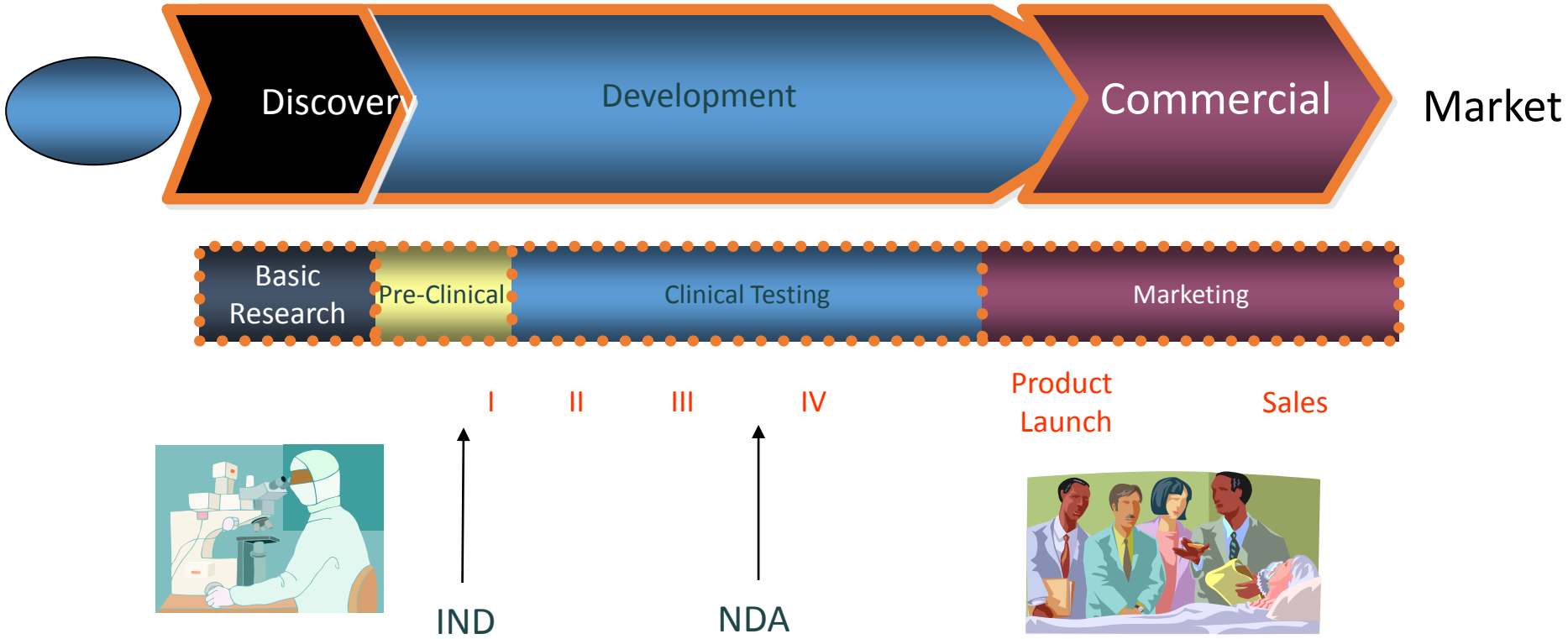
Drug Development Process



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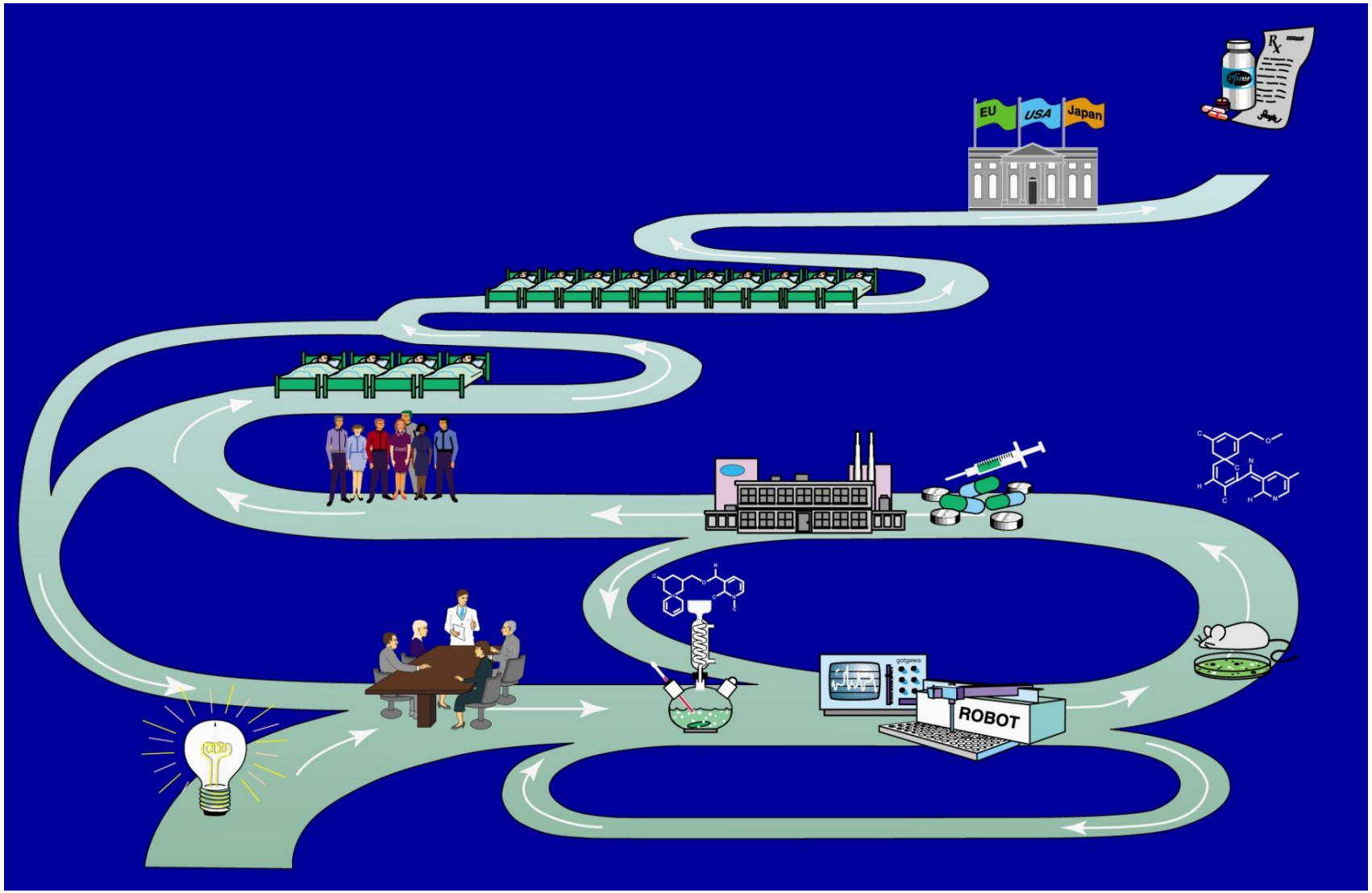
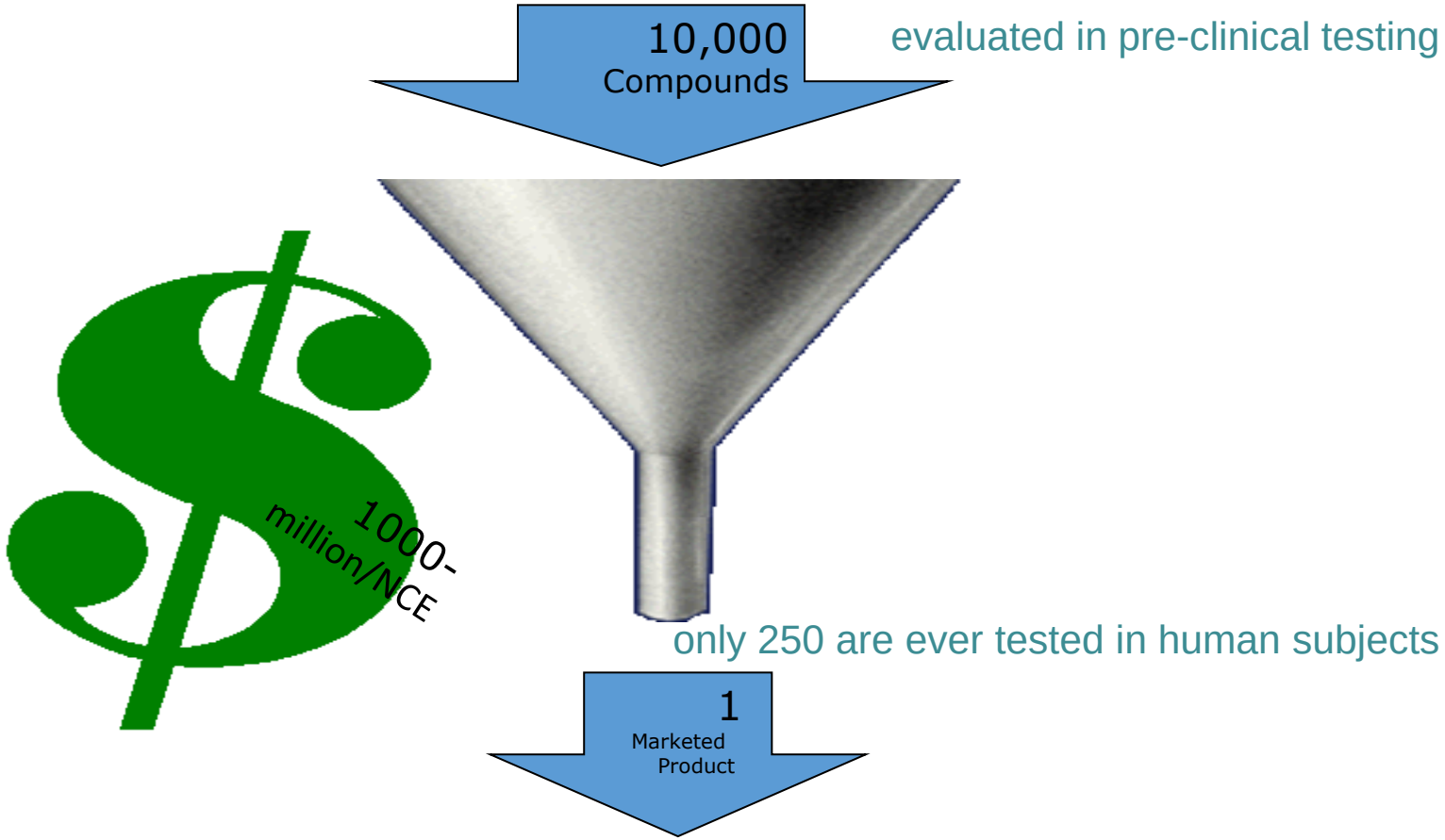
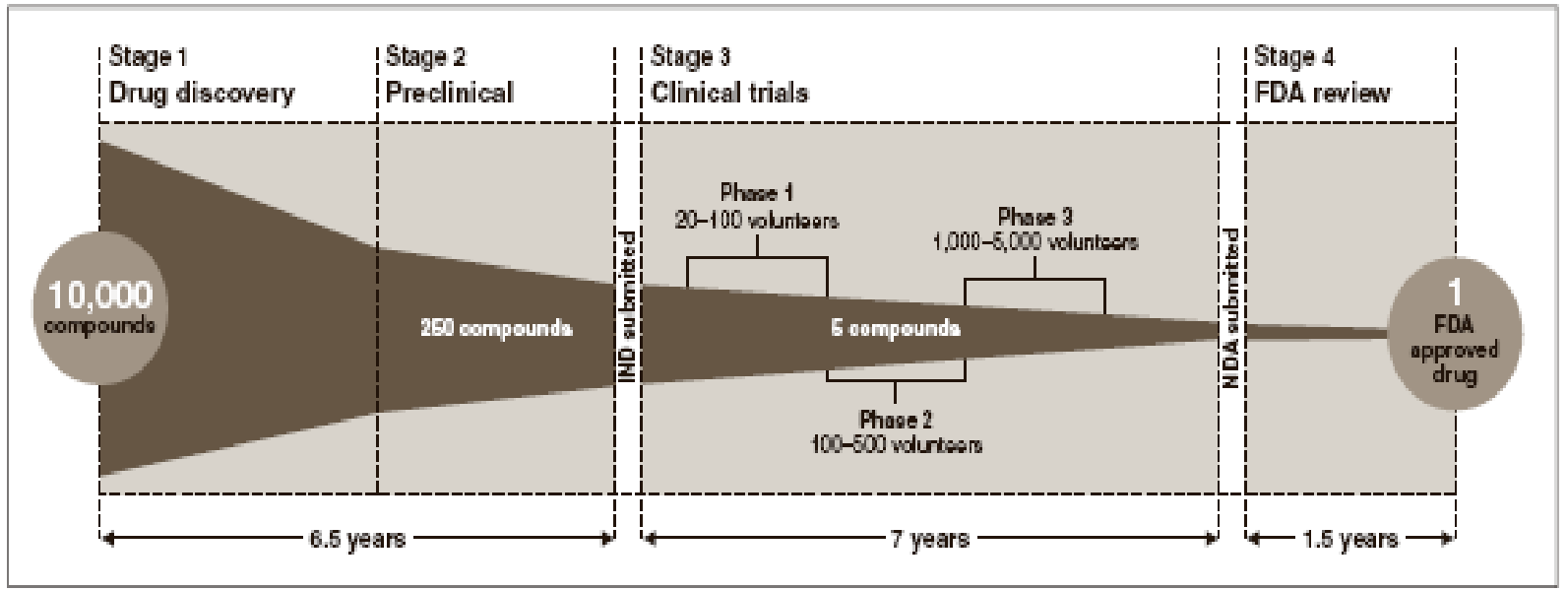


Drug Development in the U.S.



Kinetics of Drug Development Process

Figure 1: The Drug Discovery, Development, and Review Process



Source: Pharmaceutical Research and Manufacturers of America

Pharmaceutical Development

ICH Q8 (R2)

We are a start-up we don't need it!

True?

Q8 - Forward

An opportunity to present the knowledge gained through the application of scientific approaches and quality risk management (for definition, see ICH Q9) to the development of a product and its manufacturing process.

The aim of pharmaceutical development is to design a quality product and its manufacturing process to consistently deliver the intended performance of the product.

ICH Q8 (R2)

- Quality cannot be tested into products
- Quality should be built in by design

Changes in formulation and manufacturing processes during development and lifecycle management should be looked upon as opportunities to gain additional knowledge and further support establishment of the design space.

ICH Q8 (R2)

- Inclusion of relevant knowledge gained from experiments giving unexpected results can also be useful
- Design space is proposed by the applicant and is subject to regulatory assessment and approval.
- Working within the design space is not considered as a change.
- Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process.

Objectives

- Achieve Product Realization
- Establish and Maintain a State of Control
- Facilitate Continual Improvement
- Knowledge Management

Sources of knowledge include:

- Innovation
- Prior knowledge
- Pharmaceutical development studies
- Technology transfer activities
- Process validation studies over the product lifecycle
- Manufacturing experience
- Continual improvement
- *Change management* activities.

What are the key factors for success?

- Good & Commited management
- Openness to new ideas
- Focus
- Clear strategy
- Transparency with your investors and collaborators
- Risk management

Quality Risk Management

It can provide a proactive approach to:

- Identifying
- Scientifically evaluating and
- Controlling potential risks to quality.

The design, organization and documentation of the pharmaceutical quality system should be well structured and clear to facilitate common understanding and consistent application.

Risk Assessment

- The elements of cGMP should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognizing the different goals and knowledge available for each stage.
- The pharmaceutical quality system should include appropriate processes, resources and responsibilities to provide assurance of the quality of *outsource activities* and purchased materials.
- Management responsibilities should be identified within the pharmaceutical quality system.

Risk evaluation questions

Risk= Occurrence x severity x detectability

1. What is the probability it will go wrong?
2. What is the severity (consequences)?
3. Can I detect the harm easily?

Main goal of risk management

Risk control

- Process in which decisions are made and measures implemented by which risks are reduced to, or maintained within specified preferred and tolerable levels.

Management Commitment

Senior management has the ultimate responsibility to ensure an effective pharmaceutical quality system is in place in achieve the quality objectives, and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the company.

Management should:

- Participate in the design, implementation, monitoring and maintenance of an effective pharmaceutical quality system;

Management Commitment

- Demonstrate strong and visible support for the pharmaceutical quality system and ensure its implementation throughout their organization;
- Ensure that a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management.

How do you maximize the potential to develop a product?

- Experimental design
- Use high quality materials
- Repeat experiments and make sure they are reproducible
- Risk management

How do you maximize the potential to develop a product (2)

- Document, document, document…
- Provide rational for the design
- Document detailed experimental protocol
- Raw data and all calculations
- Conclusions from the experiment
- Rational for the next experiment

Development of a new product

- Basic research
- Protection of IP
- Formulation development
- Toxicological studies
- Production process development
- Production scale-up
- Production of clinical trial material (CTM)

Development of drug product- Cont.

- Development of analytical methods
- Stability studies
- Clinical trials
- Bio-analysis
- CMC
- Regulatory submission.

What have we learnt?

- GMP directives focus on patient's safety
- A start-up doesn't need to be certified
- A start-up may learn a lot from the GMP directives
- The developing organization must work in compliance with cGMP

Early stage limitations

- Scarce resources
- Limited experience in developing new drugs
- Complicated developmental process- requires expertise in many different aspects
- Limited understanding in regulatory requirements
- Impatient investors

What are the needs of most startups?

- Expertise in formulation
- Technical engineering know how
- Production knowledge and facilities
- Analytical knowledge for development and validation of procedures
- Infrastructure operating in compliance with GLP and GMP

Common Technological Limitations

- Process was developed in a small laboratory scale
- The process may not be repeated in industrial setting
- Un optimized process
- The patenting process is complicated and unclear
- Active material is expensive and thus limited

Common Technological Limitations- cont.

- Consulting many experts… some time contradicting advice
- Unclear indications
- Regulations from different authorities are confusing and demanding
- Limited knowledge about the drug product

Possible solutions

- Consult different consultants for each aspect
- Use an outsourcing one stop shop
- Establish your own laboratory
- Join an incubator

Who is Nextar ?

- Outsourcing company providing full integrated contract drug development and manufacturing (CDMO)
- Equipped with state of the art laboratories and sterile clean rooms
- Based at the Weizmann Science Park
- 33 employees

Achievements since 2007 (establishment)

- Served app. 50% of the Israeli life sciences start ups
- Over 1000 projects were performed
- Over 200 customers
- Performed various projects for Big Pharma (both local and international)
- Developed over 60 innovative manufactured for clinical trials , in Israel and worldwide

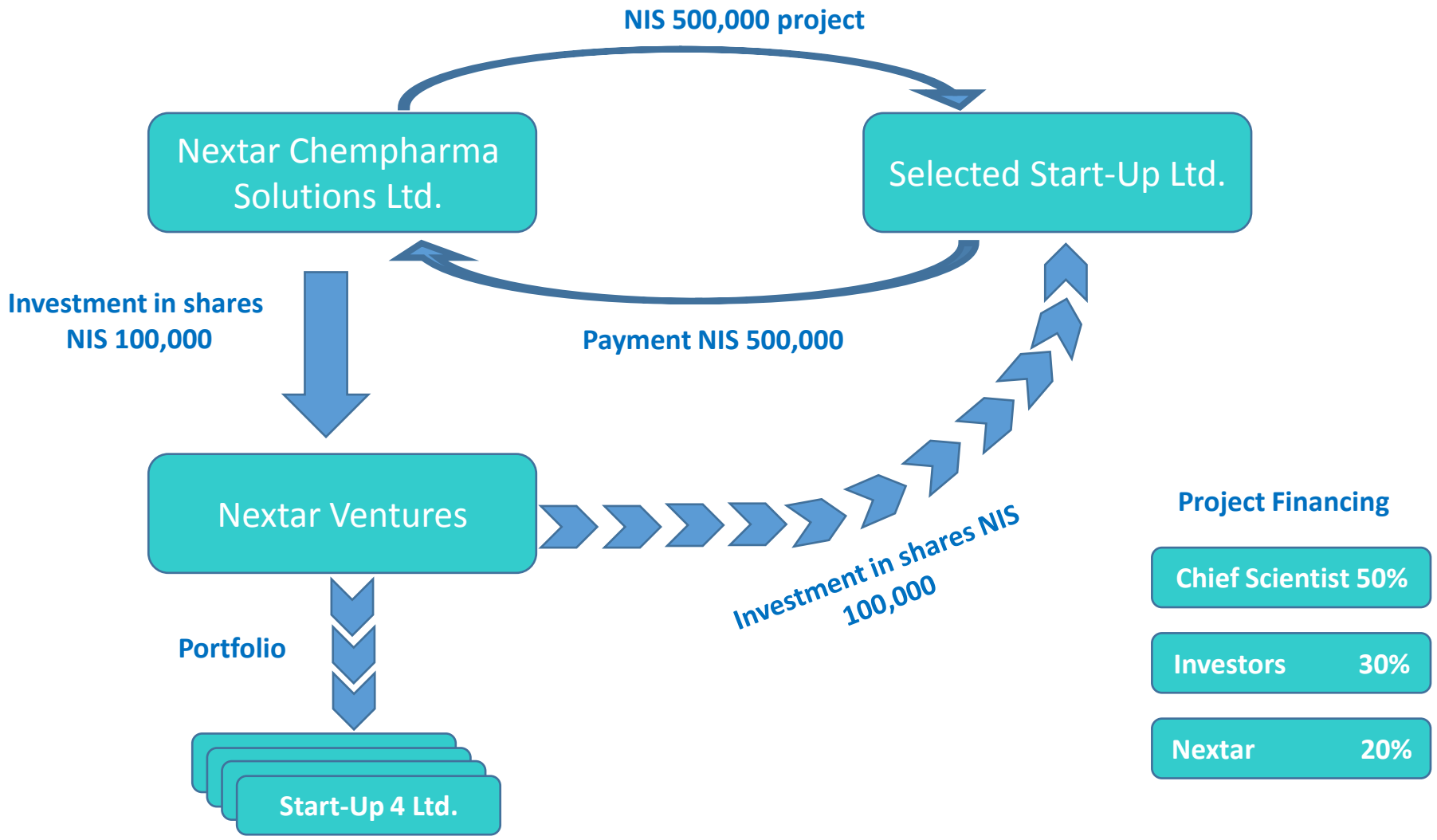
Certifications

- cGMP - by the Israeli Ministry of Health which is recognized also by EU /PIC/s
- OECD GLP
- ISO 13485 - by SII (member of IQnet)

Creating Value for investors

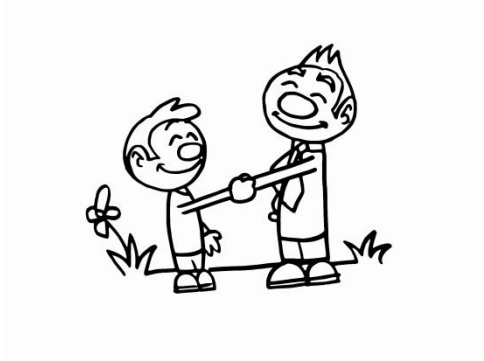
- Nextar might be interested to invest in your Start-up subject to its evaluation.
- Investment can reach 20% of a project cost (subject to the fund rules and regulations)
- Investors are required to put less capital
- Burn rate goes down, the start-up can do more with same capital
- Risk is incrementally shared

How does it work ?



Thanks for listening!

We at Nextar shall be happy to assist you



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