Project schedule for first-to-file (FTF) submission of Tucacitab in the US market

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INTAS — Expressions for a Healthy Life

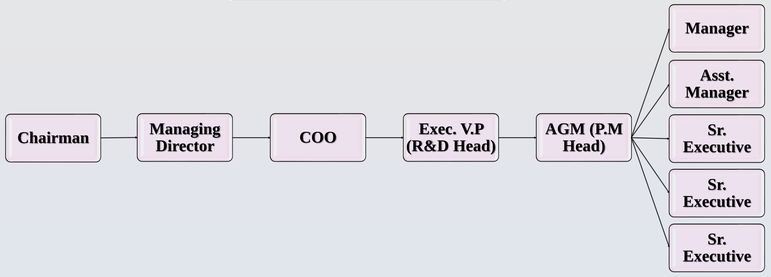
About:- **Intas Pharmaceuticals Limited** is an Indian multinational pharmaceutical company headquartered in Ahmedabad. It is a leading global pharmaceutical company with its robust product basket that includes world-class generics, oncology, biologics and parenteral as well as added-value products (AVPs). In the financial year 2019, 69% of the company's revenue came from international markets while 31% came from India.[1]

Intas has set up a network of subsidiaries as Accord Healthcare, Lambda, Astron to operate in global markets.

Mission:- Contributing to better healthcare through innovation. Maximizing value for our stakeholders and customers.

Vision:- To continually set new benchmarks in global healthcare with the power of human expertise, innovative research and advanced technology.

Organogram



Difference between practical exposure and theoretical understanding

The basic difference between theoretical knowledge and practical knowledge is that theory teaches us through the experience of others, on the other hand in practice typically pick up knowledge through our own involvement in the work in hand.

There are some reasons why Practical Wisdom is better-

- Interactive Education creates a Deeper Impact
- Involvement => Easy learning
- Develops a better understanding
- Strengthen basic understanding and technical skills
- Last but not least- It is more interesting

About Project

Project Name: TUCATINIB TABLET (50mg, 150mg) ER

Use of Tucatinib: It is a prescription medicine used to treat adults with a type of breast cancer called human epidermal growth factor receptor-2 (HER2) positive breast cancer.

Brand Name: Tukysa

Generic Name: Tucatinib

FDA Approved: Apr 17, 2020

NCE Exclusivity: Apr 17, 2025

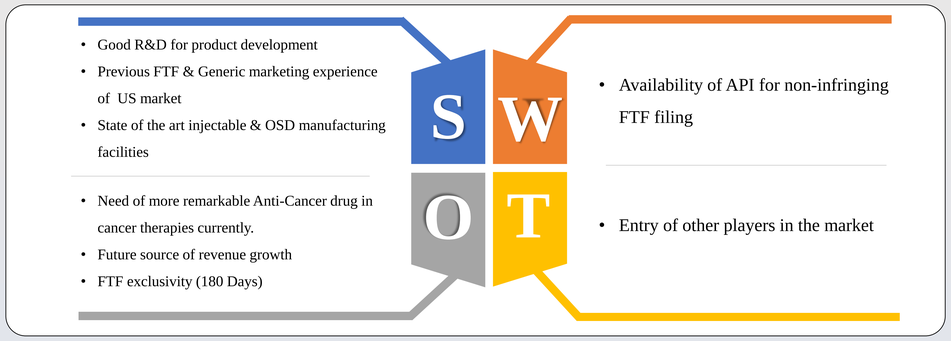
Patent Strategy: P-III/P-IV/Section-VIII

Target Market: US

Oncology Market Size- 2021

Market	USD Billion	In cr.
Total Onco Market (Global)	286.04	₹ 23,26,935.40
US (Largest market holds 46.2%)	**132.15**	**₹ 10,75,040.25**
Total Breast Cancer (Global)	28.88	₹ 2,34,938.80
US (holds 34% of TBC)	**9.82**	**₹ 79,885.70**

SWOT Analysis



Project Description

Tucatinib Tablet-50 mg,150mg
Indication: Treatment of breast cancer
Storge - (Store at) Shelf Life: 24 Months

Mfg Site: SEZ

Primary Market—US

RLD: (Tuksya),Seagen
Approval Date : 17th April-2020

Priority : A
Last Updatation Date: 29 Aug 2022

Project timeline:

Project Initiation	Prototype	Pilot Bio	SU	EB	Pivotal	Submission	Approval	Launch
April-2022	April-2023	June-2023	Aug-2023	Sep-2023	Feb-2024	Nce-1:17th-April-2024	Feb-2025	Post:April-2034

IP Timelines
Submission Date:17th April-2024
Launch :Post April-2034,with invalidation of MOU/Combination Patent
With invalidation of MOU/combination patent Revenue on launch: $ mn

IP strategy	
Earliest Filling date	NCE-1: Apr 17, 2024
NCE-1	Apr 17, 2024
API Patent Expiry	Apr 12, 2031 (PTE applied till Apr 17, 2034), Nov 16, 2024 (PTE applied till Nov 16, 2029
Other Patent	(Formulation/Polymorph) - Oct 12, 2032 (PTE applied till Apr 17, 2034) (General Formulation/MoU) - May 9, 2027 (PTE applied till Nov 29, 2028) Non-OB Patent/Patent Application: (Polymorph) - Oct 12, 2032 (MOU/Polymorph) - Oct 12, 2032 (MOU/Polymorph) - Oct 12, 2032, (MOU/Combination) - Oct 20, 2040, (Solid dispersion) - Oct 12, 2032 - Abandoned (MOU) - Mar 25, 2033 - Ready for Examination (MOU) - Mar 09, 2041 (MOU/Combination) - May 28, 2041 (MOU/Combination) - Jul 28, 2041
Patent Strategy	P-III/P-IV/Section-VIII

API Details	
Live DMF	1-Esteve Quimica SA
Live CEP	-
Primary API Source	Intas
Target Polymorph	Crystalline hemiethanolate (Form-B) or any other form
Qnty bifurcation	Dev:5Kg,SU:30Kg,EB:90Kg
Price/kg (Dev &Commercial)	$13,500/Kg

Market Intelligence	
FTF Filers	No FTF filers
ANDA Filers:	No ANDA Filers
No of players	No Players
RA Strategy	NCE-1, ANDA

COGS/%API cost	Revenue on Launch	Unit on Launch	RLD Price	Avrg Generic Price
TBC	TBC	-	150mg:$148	No Generic Player

Investment	Cost (USD)	Cost (Rs)
API(Dev , SU, EB)	$16,87,500	13,83,75,000
RLD	$86,151	70,64,382
BE Cost	$3,61,600	2,96,51,200
Litigation Expenses	$4,50,000	3,69,00,000
Regulatory	$2,00,000	1,64,00,000
Total Investment	$27,85,251	22,83,90,582

Row Labels	2021-USDMN	2022-USDMN	2021-KG	2022-KG	2021-SU-000's	2022-SU-000's	Price/Unit	% Growth $	% Growth Volume	% Growth KGS
TUCATINIB	**3.89**	**5.66**	**4.13**	**5.56**	**30.72**	**41.88**	**135.14**	**45.54**	**36.33**	**34.59**
SEAGEN INC 150MG	3.56	5.12	3.89	5.19	25.92	34.62	147.93	43.97	33.56	33.56
SEAGEN INC 50MG	0.33	0.54	0.24	0.36	4.80	7.26	74.13	62.38	51.25	51.25

Tucatinib Tablet — Technical Summary

Current Status

- API and RLD Received.
- Product development initiated.

IP Strategy

1) NI formulation strategy with replacement of Copovidone for preparation of Solid dispersion of Tucatinib.

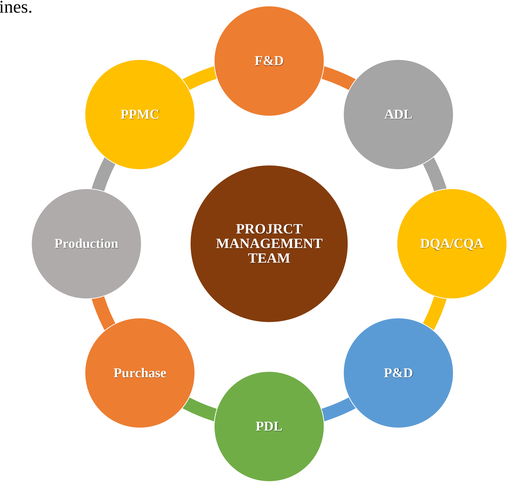
BE Study Details	
Studies required	Fasting & Fed
Pilot study design	Single-dose, two-treatment, two-period crossover in vivo
Study population	Healthy Volunteers
ISCV %	-
Pivotal studies Design	Fasting and Fed Single dose full replicate crossover
Duration	4 Months

Risk	Mitigation
RLD has used spray drying process for solid dispersion preparation for polymorphic conversion and solubility enhancement. Thus, BE is critical considering NI polymer for NI formulation.	Pilot BE with three way cross over design with two test formulation with different polymer used for preparation of solid dispersion.

API & Formulation Technical Details `	
Available Marketed Pack	US – 50 mg - Bottles of 60 tablets in 75 CC with desiccant US – 150 mg - Bottles of 60 tablets in 75 CC with desiccant & Bottles of 120 tablets in 150 CC with desiccant
Proposed Manufacturing Process	Spray Drying by top-spray granulation or HME followed by compression and film coating
Batch Size	150000 tablets of each strength
Formulation Complexity	1) Tucatinib is class II drug substance and practically insoluble in water, thus need to convert crystalline API into amorphous form with NI polymer. 2) Stability is critical considering drug substance degradation pathway.
Excipients	**Core tablet :** copovidone, crospovidone, sodium chloride, potassium chloride, sodium bicarbonate, colloidal silicon dioxide, magnesium stearate, and microcrystalline cellulose. **Yellow film coat:** polyvinyl alcohol, titanium dioxide, macrogol/polyethylene glycol, talc, and yellow iron oxide non-irradiated.
Solubility	BCS class II molecule with pH dependent solubility (Higher towards acidic pH)
Tmax:	2 hours (1 – 4 hours)
Absorption:	Tucatinib AUC_{0-inf} and C_{max} increases proportionally over a dosage range from 50 mg to 300 mg (0.17 to 1 times the approved recommended dosage). Tucatinib exhibited 1.7-fold accumulation for AUC and 1.5-fold accumulation for C_{max} following administration of TUKYSA 300 mg twice daily for 14 days. Time to steady state was approximately 4 days
Food Effect:	Administration of Tucatinib with food AUC_{0-inf} increased by 1.5 fold, T_{max} shifted from 1.5 Hr to 4 Hr and C_{max} was unaltered.
Half life:	8.5 Hours
Metabolism :	Tucatinib is metabolized primarily by CYP2C8 and to a lesser extent via CYP3A
API PSD:	Not critical considering solid dispersion technology

Learnings During Internship

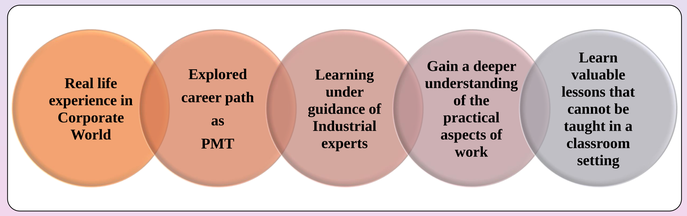
I started my internship as a Project management intern, where I learnt : i) Work and responsibilities of PMT. ii) Different types of project. iii) Dossier filing process in US, EU and India. And to understand the actual workflow, I was allowed to explore various departments, where I understood the steps of development, challenges, and how PM communicate with these departments and come-up with product lifecycle solution as per timelines.



Challenges faced during internship:

- To develop a good strategy for development of the product including-
  - Set timelines and milestone.
  - To understand work-flow of different department & role, and to understand time require for development.
  - To ensure availability of raw-materials and other necessary requirements on time during the process.
  - To ensure that every unit operation/task to be completed within stipulated timeline.
- Formula finalization using design of experiment (DOE) .
- Development & validation of analytical method as per FDA & ICH.
- To ensure the progress of product according to timeline.
- Product to be bioequivalent with RLD/RS.

Usefulness of Internship



Suggestions

Currently Tucatinib is developing for filing in US market only, we can plan to file tucatinib in EU which is 2nd largest market of breast cancer after US.