A study on identifying the Opportunities for Acquiring/ Collaborating a drug in Breast Cancer Indication

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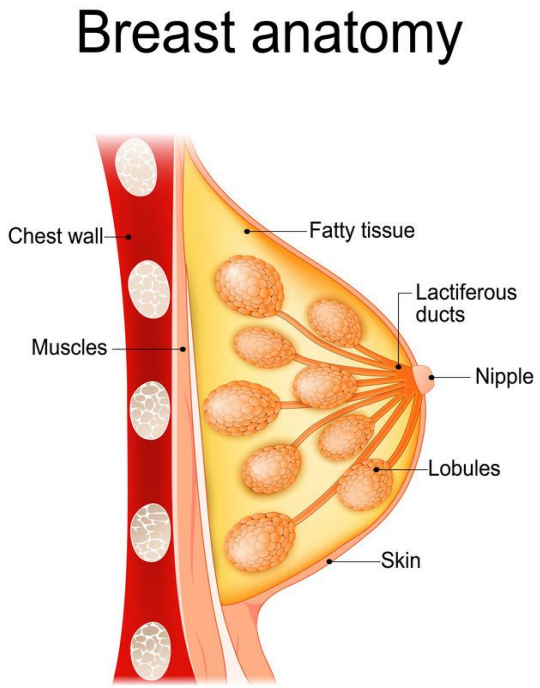
i. Disease Overview (Breast Cancer) (1/2)

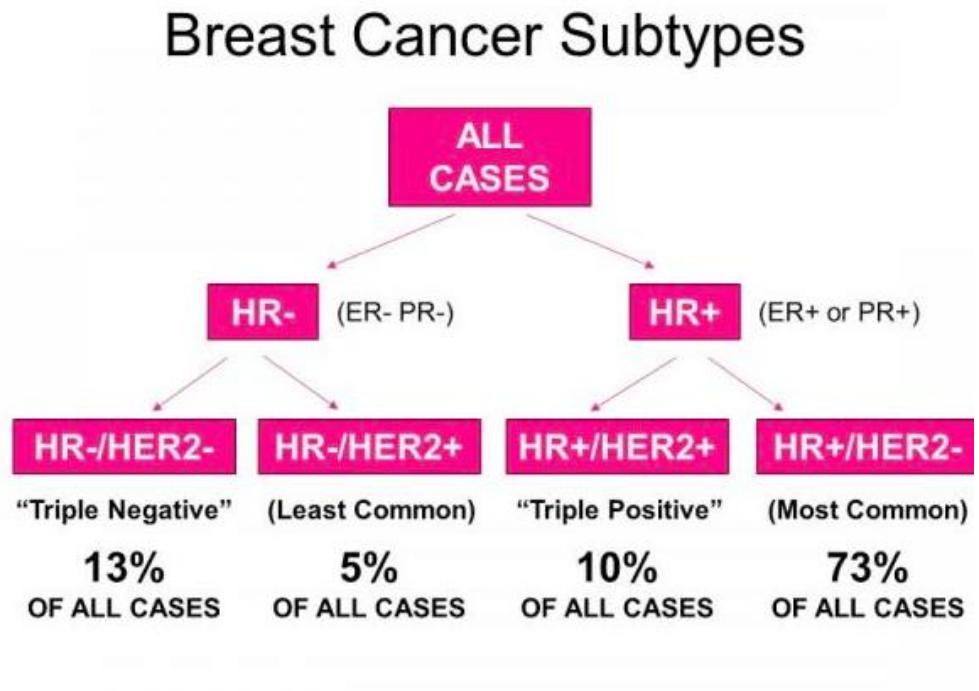
- Cancer which starts in breasts. It can begin in the duct that carry milk to nipples or in the glands that make breast milk or other tissues of the breast. And can metastasize to nearby bones affecting the skeletal system and making its way to other organs as well
- Common signs and symptoms such as Lumps; Nipple Discharge; Breast/Nipple Pain; Nipple Retraction/ Inversion; Swelling; Redness; Change in Skin texture; Lymph Node changes
- Disease progression depends upon its pathophysiology which can be Hereditary or Hormonal
    a. Hereditary- mutations in two genes, BRCA1 and BRCA2
    b. Hormonal- express oestrogen receptor and proliferate in response to oestrogen stimulation



i. Disease Overview (Breast Cancer) (2/2)

Hormonal Breast Cancer: Hormonal supply is required to develop tissue that arises out of. Breast cancer increases with lifetime oestrogen exposure. Most of breast cancers are hormone sensitive, i.e. they express oestrogen receptors and proliferate in response to oestrogen stimulation.

- Estrogen receptor (ER) positive. The cells of this type of breast cancer have receptors that allow them to use the hormone estrogen to grow. Treatment with anti-estrogen hormone (endocrine) therapy can block the growth of the cancer cells.
- Progesterone receptor (PR) positive. This type of breast cancer is sensitive to progesterone, and the cells have receptors that allow them to use this hormone to grow. Treatment with endocrine therapy blocks the growth of the cancer cells.
- Hormone receptor (HR) negative. This type of cancer doesn't have hormone receptors, so it won't be affected by endocrine treatments aimed at blocking hormones in the body.
- HER2(human epidermal growth factor receptor 2) is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher than normal levels of HER2 are called HER2-positive.



ii. Rationale

- Oncology is one of the most lucrative and R&D heavy industries now a days with most major companies competing to find the cure of one of most deadly diseases that the mankind is facing
- Billions of dollars are spent annually for the research and development of these molecules. And billions are spent on them annually by the care seekers fighting the disease.
- In 2017, there were an estimated 3,577,264 women living with female breast cancer in the United States.
- Approximately 12.9 percent of women will be diagnosed with female breast cancer at some point during their lifetime.
- The rate of new cases of female breast cancer was 128.5 per 100,000 women per year. The death rate was 20.3 per 100,000 women per year (SEER,2020).
- 1 in eight women in US will develop breast cancer once in her lifetime.
- This growing demand motivate US Pharmaceutical firms to pursue business development opportunities in this indication.

iii. Aim:

To identify the Opportunities for Acquiring/Collaborating a drug in Breast Cancer Indication.

iv. Objective:

a) To study the Competitive landscape of molecules in Breast Cancer Market
b) To analyze the Opportunities for acquiring/ collaborating in Breast Cancer
c) To determine the key products and players in the Breast Cancer Market

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Methodology

- RESEARCH QUESTION: What are the Opportunities for Acquiring/Collaborating a drug in Breast Cancer Indication?
- STUDY DESIGN- Descriptive Exploratory study
- PERIOD OF STUDY– February 2020 to May 2020
- STUDY AREA- U.S. pharmaceutical market
- DATA COLLECTION TECHNIQUE- Review of relevant documents has been done and qualitative information was collected based on resources inputs provided.
- DATA SOURCE-Secondary sources include CT.gov; AdisInsight; Google Scholar; Pub-med; Evaluate Pharma reports; ASCO (American Society of Clinical Oncology); AACR (American Association for Cancer Research)

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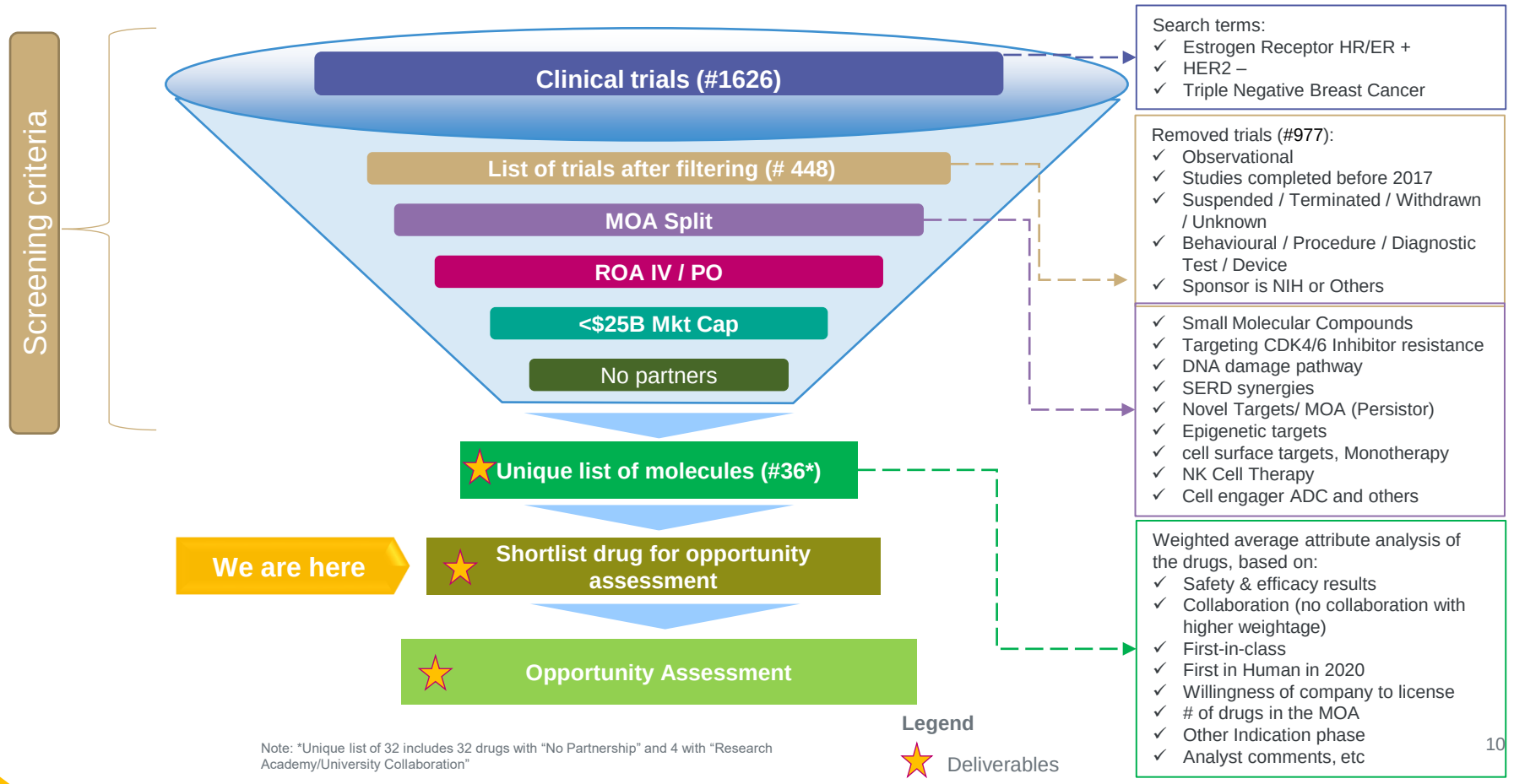
Screening Criteria



Note: *Unique list of 32 includes 32 drugs with "No Partnership" and 4 with "Research Academy/University Collaboration"

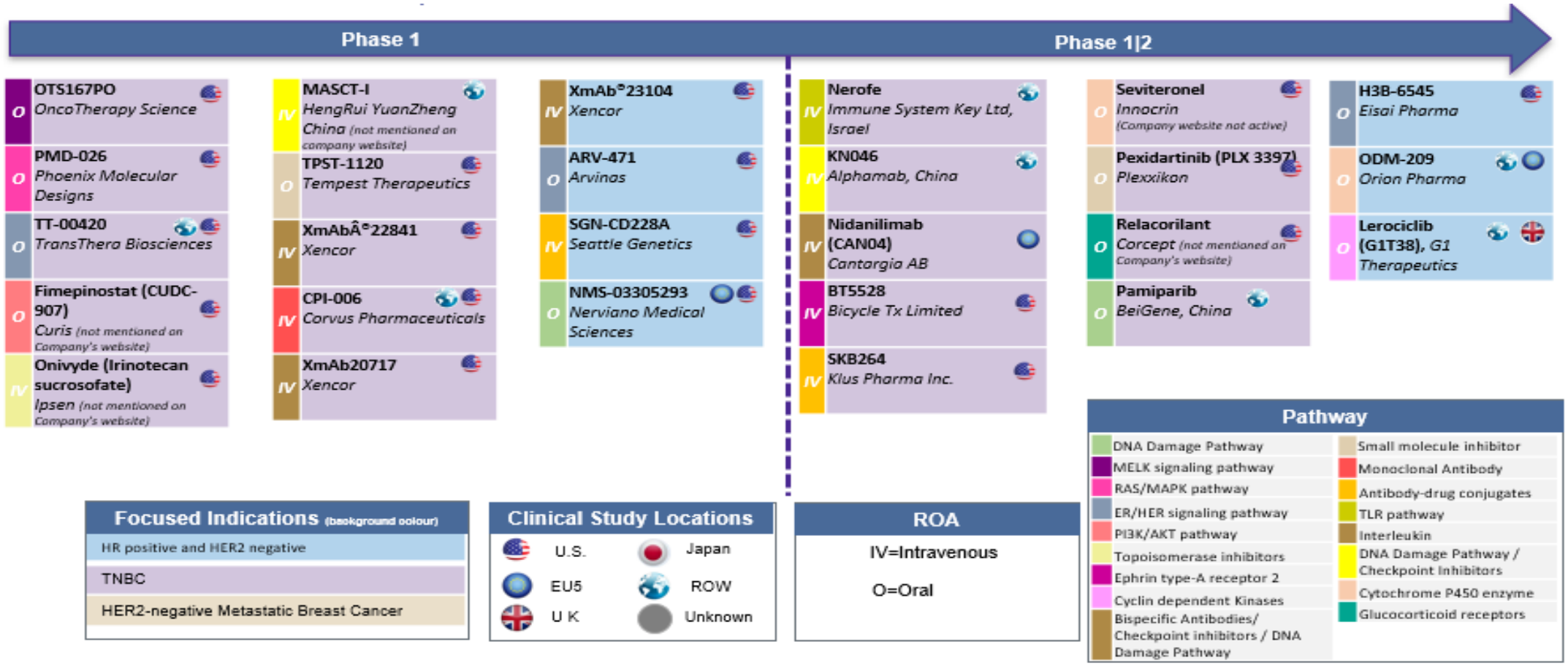
• Key Findings

This table depicts the churned outcome of the rigorous screening method employed in the previous steps.
And a Cut of Market capital less than $25 Billon was applied to select small companies to whom collaboration or acquirement would be easy.
Out of which 32 molecules were those who have no partnership at all, and 4 molecules were those which has any university or Research academy collaboration. As a result of which 36 molecules of interest were found.

Categories	**#**
Triple Negative Breast Cancer trials	701
Estrogen Receptor-positive Breast Cancer trials	383
HER2-negative Breast Cancer trials	542
TOTAL	1626
Duplicate trials	201
Unique trials	1425
Observational trials	103
Terminated/Withdrawn/Unknown/Suspended trials	244
Completed before 2017 trials	257
Sponsors Other/NIH trials	326
Procedure/Behavioral/Test trials	11
Not in scope, duplicate drugs in early stage	36
Total excluded trials	977
Total to be cleaned trials	448
Focused MOA	392
IV & Oral	360
MCAP <$25Bn	75
No partnership	32
Yes (Research Academy/University Collaboration)	4
Yes (Clinical Trial Collaboration)	21
Yes (Product/Regional commercialization/in-licensed)	18

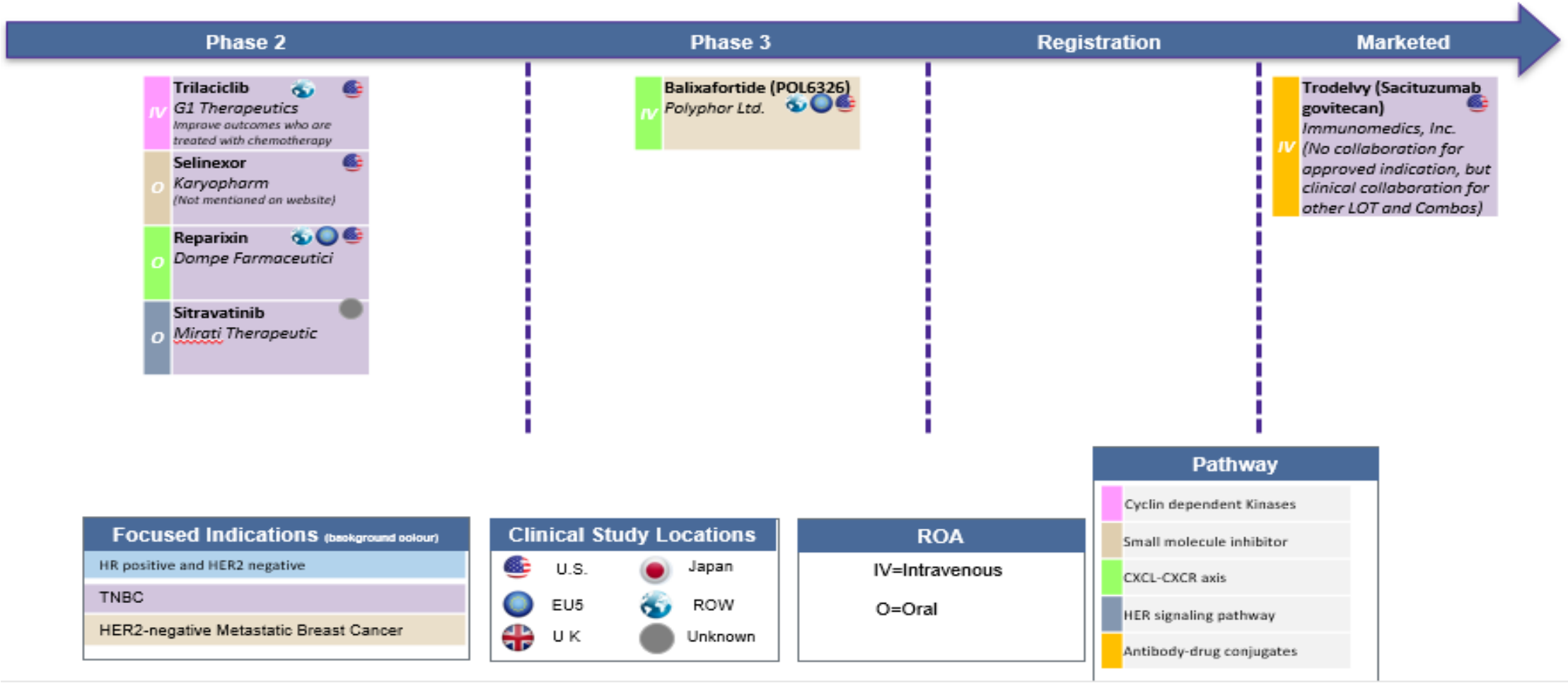
C.I. Landscape of Early Stage No Partnership Drugs (out of 32 molecules) (1/3)

There are 14 molecules in Phase-1 and 12 molecules in Phase 1|2 and most of them are studied in TNBC



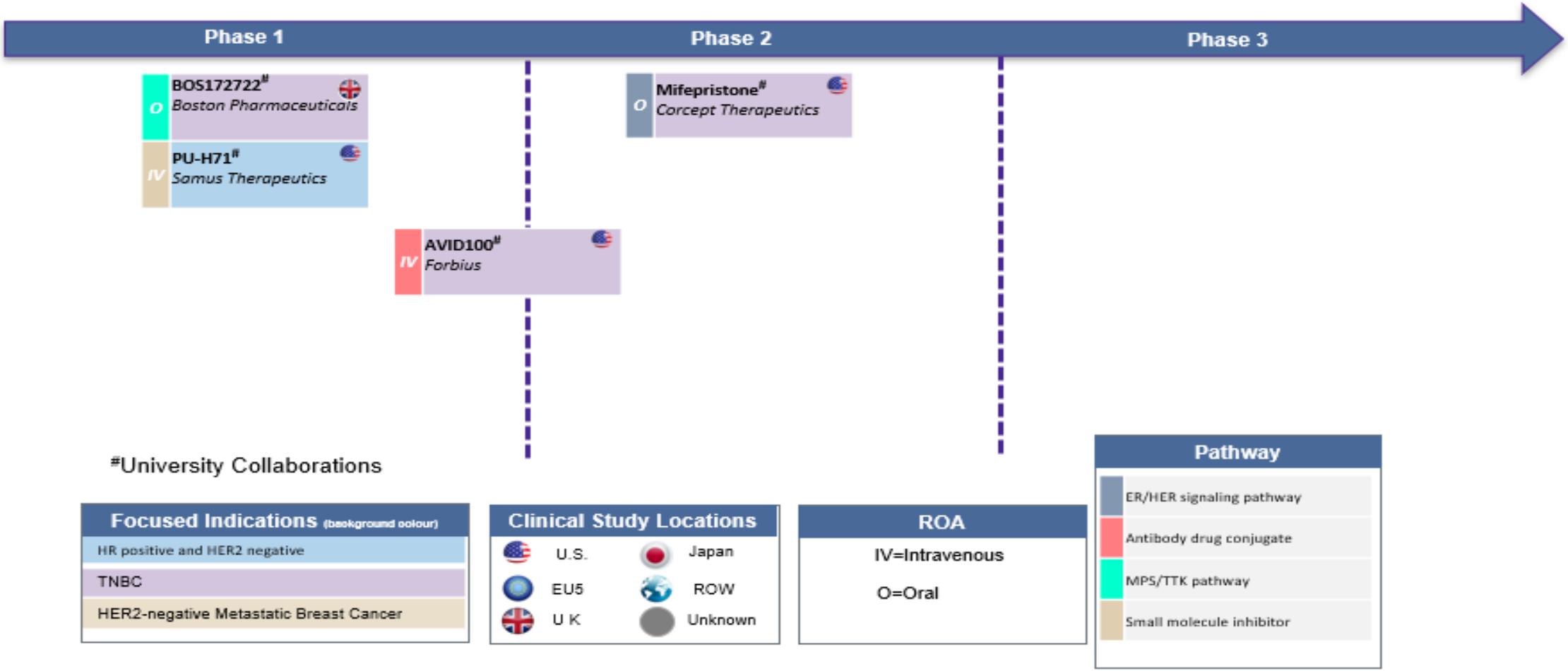
C.I. Landscape of Early Stage No Partnership Drugs (out of 32 molecules): (2/3)

There is one marketed drug, one molecule in Phase-3 & four in Phase-2 stage of development for TNBC and HR+/HER2-



C.I. Landscape of drugs in research collaborations with Universities: (3/3)

There are four molecules which are studied in TNBC & HR+/HER2- patients with university collaboration



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Attribute Analysis (Company) (1/2)

Sr no	Focused Parameters	Rationale	Weightage	Score	Potential sub-parameters	Illustration	Filters
1.	**Mcap >$25Bn**	Division between Big Pharma and Mid-Small companies	-	-	Yes	Capivasertib (*AstraZeneca)*	*Excluded*
				-	No	Trilaciclib (G1 Therapeutics)	***Included***
2.	**Collaboration**	To identify opportunities, can be about innovation, sponsored research or combination therapy to use it in treatment	**10%**	3	No	NMS-03305293 (Nerviano Medical)	***Included***
				2	Collaboration in different LOT in TNBC/HR+/HER2-	Trodelvy (Seattle Genetics)	***Included***
				1	Collaboration with university/ Research academy	Avid 100 *In research collaboration with National Research Council, Canada*	***Included***
				-	Yes *(In-licensed)*	S81694 *Product of NMS group, In-licensed with Servier*	*Excluded*
				-	Yes *(Regional Commercialization)*	Olinvacimab (SSS-23) *Product of PharmAbcine, partnered with Asia 3SBIO*	*Excluded*
				-	Yes *(Co-development)*	Camidanlumab tesirine (ADCT-30) *ADC therapeutics and Genmab are co-developing*	*Excluded*
				-	Yes *(Clinical Trial Collaboration)*	ZEN3694 *Product of Zenith Epigenetics is in trial collaboration with Pfizer*	*Excluded*

Attribute Analysis (Company) (2/2)

Sr no	Focused Parameters	Rationale	Weightage	Score	Potential sub-parameters	Illustration
3.	**Willingness of company to License**	To identify how inclined a company is to partner/ collaborate	**15%**	3	High	Lerociclib (G1T38) *Company mentioned in SEC filings:* *"Exploring partnering opportunities to continue to advance clinical development of lerociclib"*
				2	Medium/Moderate	BT5528 *(For different portfolio they partnered with Genentech, hence will look for partners)*
				1.5	Insufficient Information	Seviteronel (Innocrin Pharmaceutical) (Company's website not active)
				1	Low	Onivyde (Irinotecan sucrosofate) *(Already commercialized in other indications)*
4.	**Clinical development status of the drug**	Status of drug in development phase as mentioned on company's website	**10%**	3	Ongoing Trial and Active on website	AVID100 *(Molecules and BC indication mentioned on website)*
				2	Mentioned on company website or clinical trials as Solid tumors (covers TNBC/HER2-/HR+)	SGN-CD228A *(mentioned on website as solid tumors- no focused indication)*
				1	Company website is not active, but trial is active	Seviteronel (Innocrin Pharmaceutical) (Company's website is inactive, but trial is active on Clinical trials.gov)

Attribute Analysis (Molecule) (1/4)

Sr no	Focused Parameters	Rationale	Weightage	Score	Potential sub-parameters	Illustration
1.	**First-in-class**	Drugs that use a new and unique mechanism of action for treating a medical condition according to FDA 2011 Novel New Drugs	10%	3	Yes	Trilaciclib *("First in class" CDK 4/6 Inhibitor)*
				0	No	CPI-006
2.	**# of drugs with same MOA**	To determine the uniqueness of the molecule, based on how many drugs are acting with same mechanism	10%	3	None	H3B-6545 *(First-in-Class)*
				2	Drug with dual MOA	XmAbÂ®22841* *(CTLA-4 & LAG-3 targeted bispecific antibody)*
				1.5	One to three	CPI-006* *(Two others)*
				1	Four to Six	NMS-03305293* *(Six others)*
				0	More than 6	ARV-471*
3.	**First-in-Human 2020**	Project scope mentioned to focus on First in Human 2020 drugs **(Excluded in Late stage molecules)**	15%	3	Yes	SKB264 *(Actual study start date was Feb 28, 2020)*
				1.5	No, but First in 2019	PMD-026 *(Actual study start date was Nov 14, 2019)*
				0	No	Fimepinostat (CUDC-907) *(Actual study start date was Nov-2014)*
4.	**Studies in other Indication Phase**	Other conditions in which the molecules is studied to discern future scope	5%	3	Yes (irrespective of phase & # of indications)	OTS167PO (Acute Myeloid Leukemia –P1)
				0	No	H3B-6545

Attribute Analysis (Molecule) (2/4)

Sr no	Focused Parameters	Rationale	Weightage	Potential sub-parameters	Score	Illustration
5.	**Efficacy**					
	a) Early mid stage molecules	Based on pre-clinical anti-tumor activity on Xenografts models	30%	i. Tumor Growth Inhibition (TGI) ii. Tumor Volume Reduction (TVR)	3- Positive Quantified study results in Breast Cancer	OTS167PO
					2- Positive Qualitative study results in Breast Cancer	SGN-CD228A
					1- Positive results in other indications	Fimepinostat (CUDC-907)
					0- No Information available	SKB264
		It is a sum of Complete response + partial response + Stable disease thus reflecting anti tumor effect of drug	70%	i. Complete Benefit Rate (CBR)	3 - >=50% in Breast cancer	H3B-6545 (56%)
					2 - >30% and <50% in breast cancer and >50% in another indication	Seviteronel (33% in TNBC)
					1- <=30% in breast cancer or <50% in another indication	Selinexor (30%)
					0- If no information is available	ODM-209

Attribute Analysis (Molecule) (3/4)

Sr no	Focused Parameters	Rationale	Weightage	Potential sub-parameters	Score	Illustration
5.	**Efficacy**					
	b) Late and Registration stage molecules	In later stages, CBR has minimal implication on Clinical Benefit	15%	Complete Benefit Rate (CBR)	3 - More than 50% in Breast cancer	Balixafortide (POL6326) (63%)
					1.5 - Less than 50% in breast cancer	Trodelvy (Sacituzumab govitecan) (IMMU-132) (45.4%)
					0 - no results	-
		Primary endpoints that FDA believes to be most appropriate measure of Clinical Benefit	50%	Median Overall Survival (Median OS)	3 - 12 to 18 months	Balixafortide (POL6326) (18 months) Trodelvy (Sacituzumab govitecan) (IMMU-132) (13 months)
					2 - 6 to 12 months	-
					1 - 0 to 6 months	-
		Primary endpoint in evaluating treatment of metastatic cancer (PFS is often used as surrogate endpoint to Median OS)	35%	Progression Free Survival (PFS)	3 – 1+ year	-
					1.5 – 3 to 12 months	• Balixafortide (POL6326) (6.2 months) • Trodelvy (Sacituzumab govitecan) (IMMU-132) (5.5 months)
					0 - <3 months	-

Attribute Analysis (Molecule) (4/4)

Sr no	Focused Parameters	Rationale	Weightage	Potential sub-parameters	Score	Illustration
6.	**Safety**	Molecules achieves significant safety levels as compared to placebo in the subjects	10%	Positive data from clinical stage	3	H3B-6545 *No dose-limiting toxicities and only one Grade 3 treatment related adverse event (TRAE) have been observed (lymphocyte count decrease)*
				Positive data from preclinical stage	2	KN046 *Good safety, tolerability and preliminary efficacy*
				No data found but drug is in clinical stage	1	PU-H71
7.	**Analyst Comments**	Industry experts / KOLs mentioning or commenting on the drug / company **(Included in Late stage molecules)**	5%	Positive	3	Balixafortide (POL6326)
				Neutral	2	-
				No comments	1	-
				Negative comments	0	-

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Results of Early-mid stage molecules

Top 7 products from Attribute Analysis of Early-mid stage molecules Scored =>2

Rank	Scores	Molecule Names
1	2.3	H3B-6545 (Eisai Pharma)
2	2.2	Trilaciclib (G1 Therapeutics)
3	2.2	PMD-026 (Phoenix Molecular Designs
4	2.1	TPST-1120 (Tempest Therapeutics)
5	2.1	ODM-209 (Orion Pharma)
6	2.0	OTS167PO (OncoTherapy Science)
7	2.0	BT5528 (Bicycle Tx Limited)
8	1.9	Lerociclib (G1T38) (G1 Therapeutics)
9	1.9	Reparixin (Dompe Farmaceutici)
10	1.9	Nerofe (Immune System Key)
11	1.9	Selinexor (Karyopharm)
12	1.9	Sitravatinib (Mirati Therapeutic)
13	1.9	Pamiparib (BeiGene)
14	1.8	Pexidartinib (PLX 3397) (Plexxikon)
15	1.8	KN046 (Alphamab)
16	1.8	Nidanilimab (CAN04) (Cantargia AB)
17	1.8	TT-00420 (TransThera Biosciences)
18	1.8	SKB264 (Klus Pharma)
19	1.6	NMS-03305293 (Nerviano Medical Scie
20	1.6	PU-H71 (Samus Therapeutics)
21	1.6	Fimepinostat (CUDC-907) (Curis, Inc.)
22	1.6	Relacorilant (Corcept Therapeutics)
23	1.5	XmAb®23104 (Xencor)
24	1.5	ARV-471 (Arvinas Inc)
25	1.5	Onivyde (Irinotecan sucrosofate) (Ips
26	1.4	CPI-006 (Corvus Pharmaceuticals)
27	1.4	SGN-CD228A (Seattle Genetics)
28	1.3	XmAbÂ®22841 (Xencor)
29	1.3	XmAb20717 (Xencor)
30	1.3	AVID100 (Forbius)
31	1.3	Seviteronel (Innocrin)
32	1.1	Mifepristone (Corcept Therapeutics)
33	1.1	BOS172722 (Boston Pharmaceuticals)
34	1.0	MASCT-I (HengRui YuanZheng)

Results of Late stage molecules

Top 2 products from Attribute Analysis of Late stage molecules Scored =>2

Late stage products		
Rank	Scores	Molecule Names
1	2.7	Balixafortide (POL6326) (Polyphor)
2	2.3	Trodelvy (Sacituzumab govitecan) (IMMU-132)

Results

Top 2 products from Attribute Analysis of Late stage molecules Scored =>2

Late stage products		
Rank	**Scores**	**Molecule Names**
1	2.7	Balixafortide (POL6326) (Polyphor)
2	2.3	Trodelvy (Sacituzumab govitecan) (IMMU-132)

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Conclusion

- The study began with 1626 clinical trials out of which we identified 1425 unique trials. After which a carefully crafted screening criteria was applied, and 36 molecules promising molecules were found as a result having no partnerships.
- These 36 molecules were again put to test using a deep dive attribute analysis in which scores and weightages were allocated to different attributes.
- As the result of this rigorous exercise a total of **9 molecules** were identified at the end fitting into the set criterions which were defined in the beginning of this project out of which **2 were in late stage development (Balixafortide; Todelvy)** and **7 were in early-mid stage of development (H3B-6545; Trilaciclib; PMD-026; TPST-1120; ODM-209; OTS167PO; BT5528).**
- Now the study findings would be utilized by client to review our top products and define their interest molecules.

Thankyou