

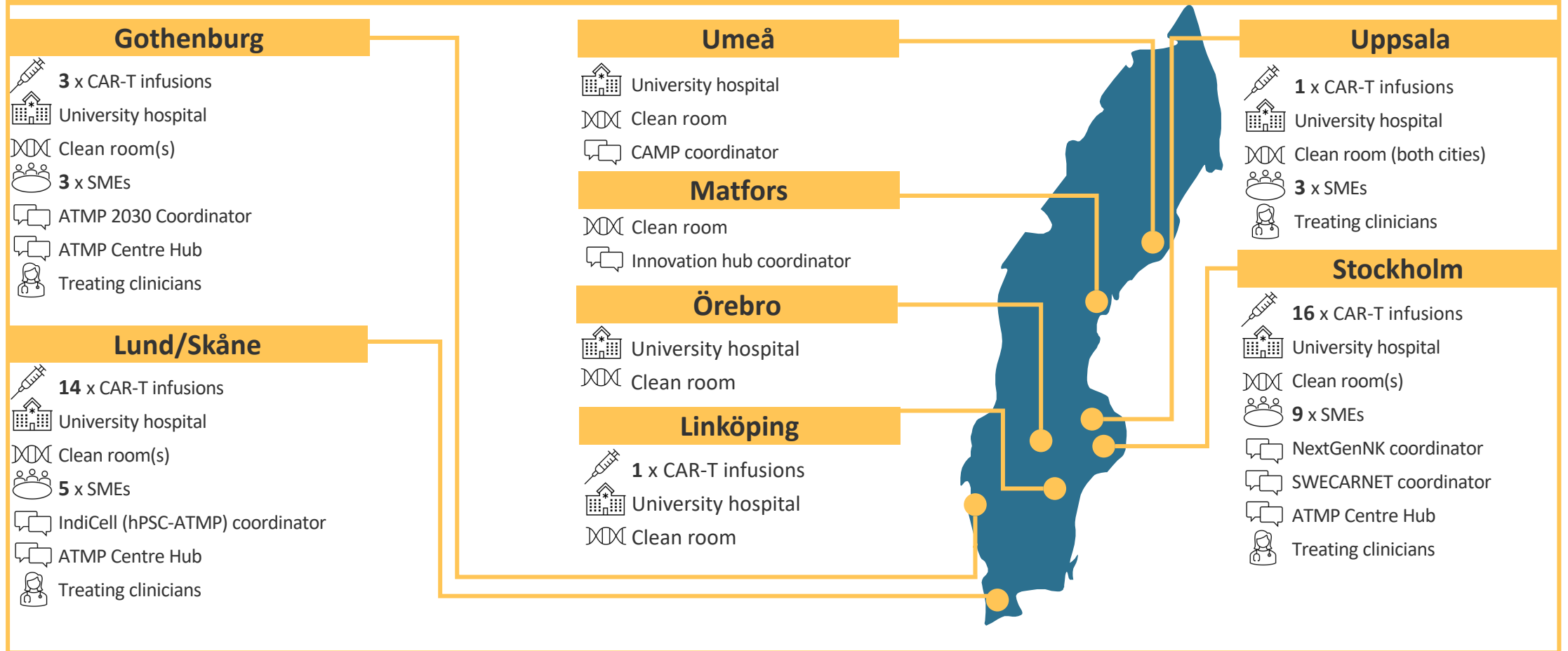
**ATMP
Sweden**

**Yearly Report
May 2022**

Executive summary/summarizing pictures

The largest ATMP cluster in Sweden is in Stockholm

Overview of ATMP related activities in Sweden



Sources: MSC analysis based on ATMP survey and publicly available data

To capture the status of the Nordic ATMP landscape a survey was conducted

- To capture the current status of the Nordic ATMP landscape a survey among ATMPs was conducted as input to the first Nordic ATMP Annual Report.
- The survey has been sent out to all identified companies active in advanced therapies, in Sweden, Norway, Denmark and Finland.
- In total 19 biotech SMEs and six international companies responded to the survey, as well as regions that responded with their CAR-T infusions.
- The main focus of the annual report will be on the SMEs. There will be separate parts about the answers of international companies.
- Good to mention: Since this is the first year of the annual report, the hope is that there will be a larger awareness of the creation of the report for next year's edition – resulting in a more complete status update of the Nordic landscape.

Identified companies with ATMP activity in the Nordic region

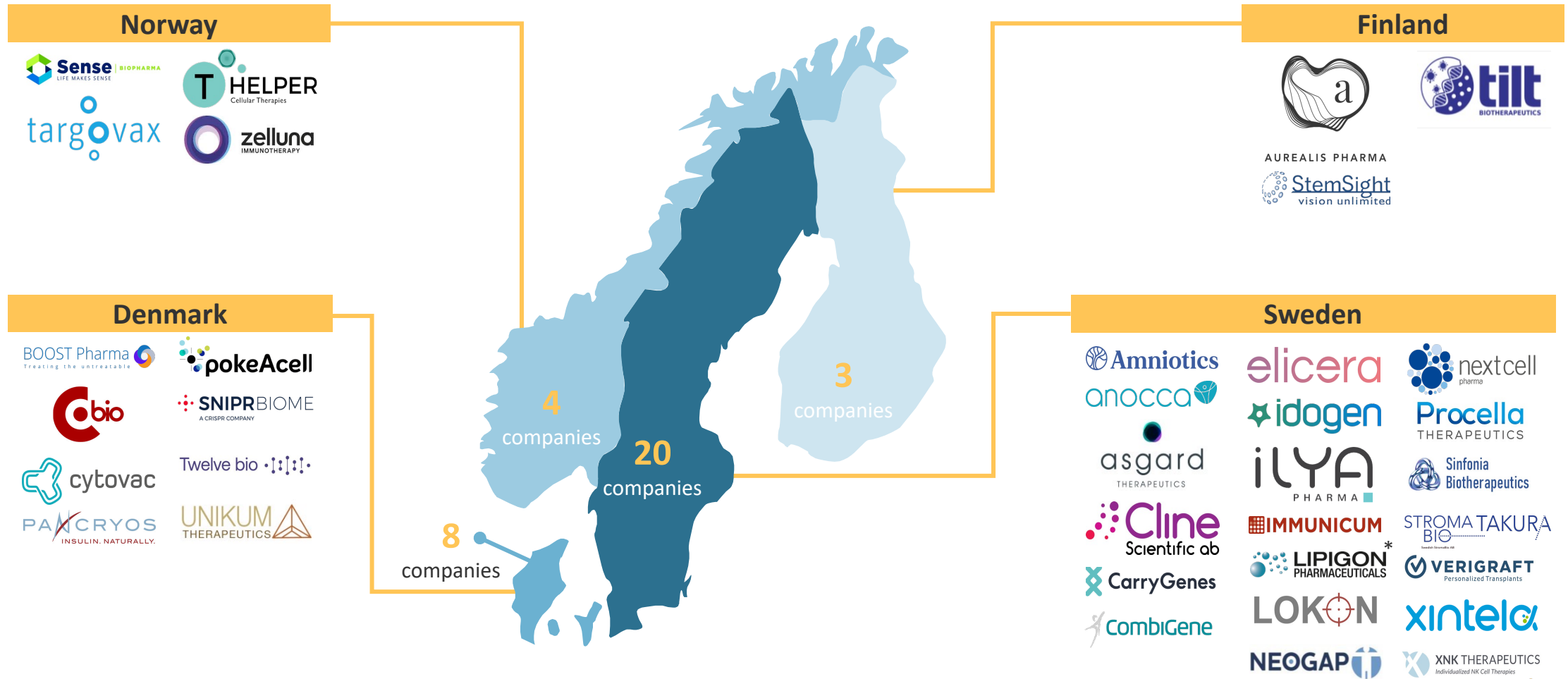
Is your company missing? Contact us!

Nordic SME companies		
Amniotics	Ilya Pharma	StemSight
Anocca	Immunicum	Takura
Asgard Therapeutics	Lipigon	Targovax
Aurealis pharma	Lokon Pharma	Thelper AS
BOOST Pharma	Neogap (TCER AB)	TILT Biotherapeutics Ltd
Carry Genes	Nextcell Pharma	Twelve Bio
Cbio	Pancryos	Unikum
Cline Scientific	PokeAcell	Verigraft
CombiGene	Procella Therapeutics	Xintela
Cytovac	Sense Biopharma	XNK Therapeutics
Elicera	Sinfonia Biotherapeutics	Zelluna
Idogen	SNIPR Biome	
International companies with ATMP activity in the Nordic Region		
AstraZeneca	Janssen	Pfizer
Bristol-Myers Squibb	Kite	Roche
CSL Behring	Novartis	Sarepta

The SME companies are defined by being founded and having their main operating activity in the Nordics. The maturity level varies, but all have development programs in preclinical or clinical stage and have no marketed products.

Focus on SMEs

57% of the 35 identified ATMP companies are located in Sweden



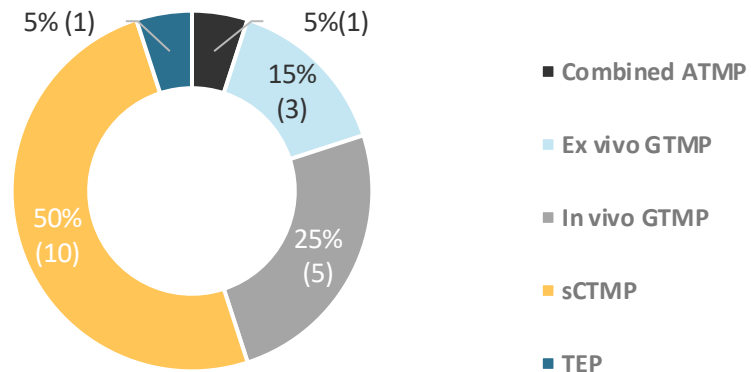
* Lipigon's only ATMP asset has been outlicensed to Combogene

Sources: MSC analysis based on ATMP survey and publicly available data

The Swedish landscape is dominated by companies active in sCTMP



Main focus area of Swedish ATMP companies (n = 20)



- A deep dive into the focus areas of the Swedish companies reveal that the sCTMP field is the largest in terms of number of SME companies.

Of the responding SMEs, a majority is located in Sweden

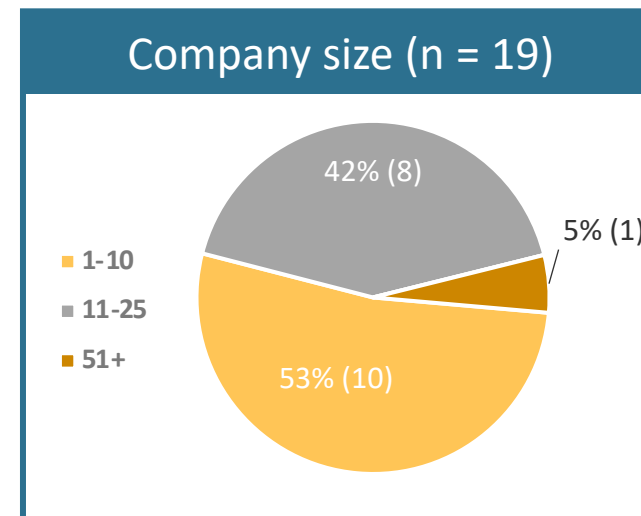
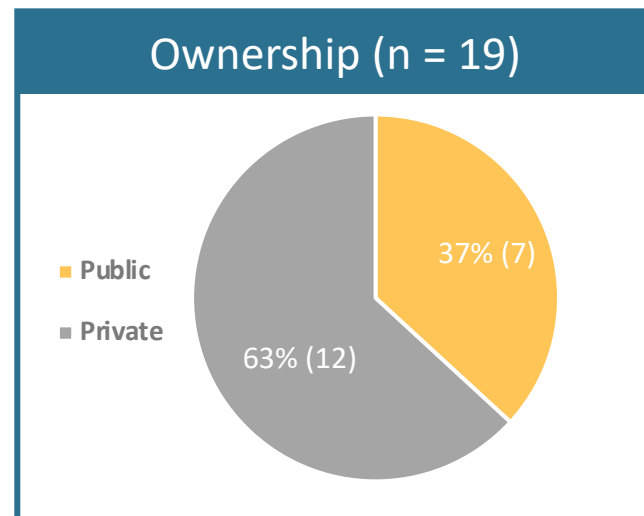
- These are the 19 SMEs that have responded to the survey.
- Note that Stroma Bio, a wholly owned subsidiary of Takura, responded to the survey, and not Takura itself.



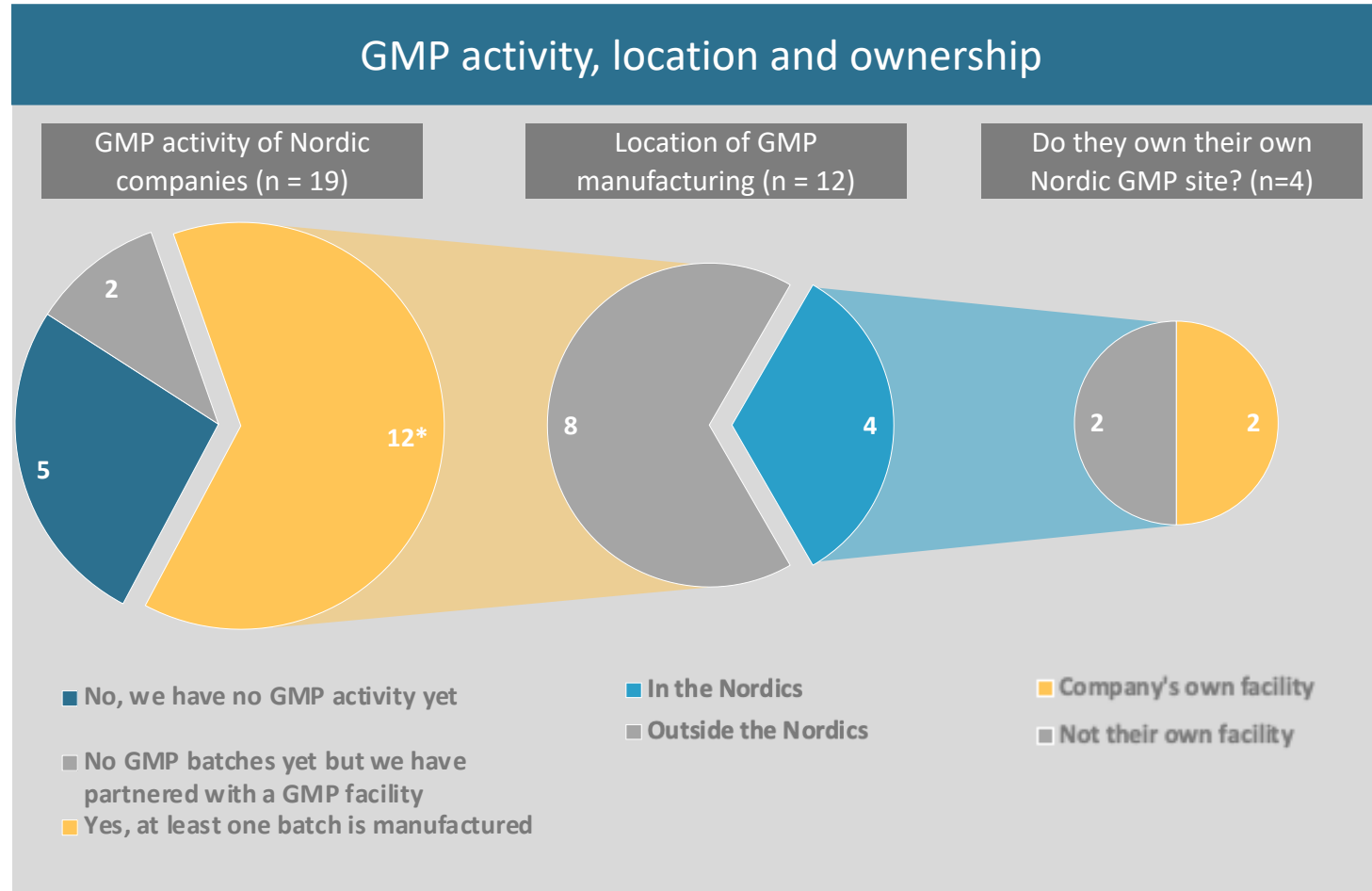
Sources: MSC analysis based on ATMP survey

Most companies have up to 25 employees and 37% are publicly traded

- All survey responding SMEs but one have <26 employees. One company has more than 51 employees.
- No company answered that their size was between 25 and 50 employees.
- Interestingly, 37% of the biotech companies are publicly traded, although 95% have less than 26 employees.



Two Nordic SMEs run their own GMP site

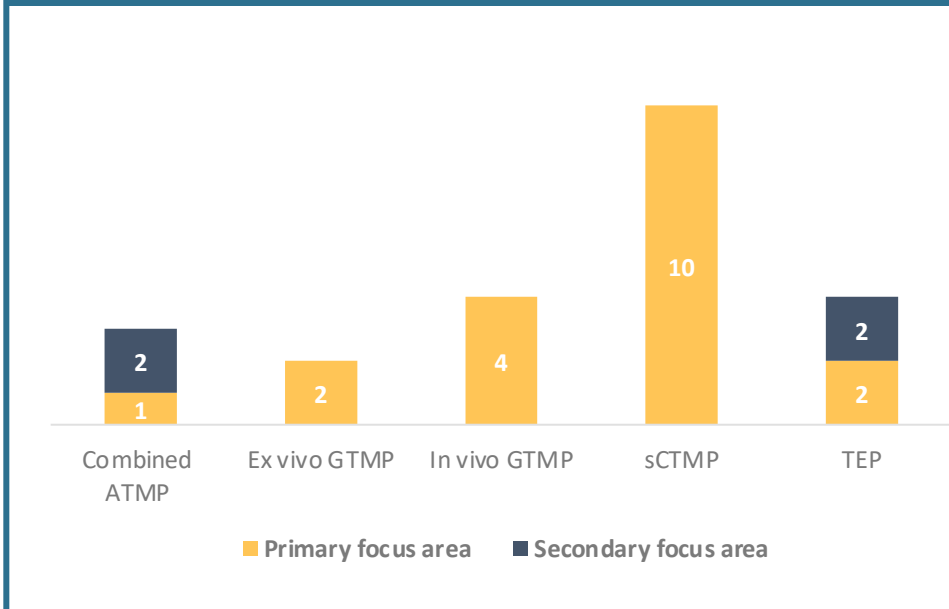


- Of the total 12 companies that had produced at least one GMP batch, 4 of them had production in the Nordic region.
- The remaining 8 companies had production in the following locations:
 - 2 in the EU/Europe, excluding the Nordics
 - 1 undisclosed, excluding the Nordics
 - 1 in both Germany and the US
 - 2 in Spain
 - 1 in the Netherlands
 - 1 in the US
- Of the 4 companies that had production in the Nordics, 2 of them owned the facility themselves. The two other manufactured their GMP batch(es) in the Vecura site in the Karolinska University hospital in Huddinge.
- There are two companies that have entered a partnership but do not have any batches yet. They have partnered with Cellcolabs and Vecura respectively. The companies have both validated their processes and developed validated analysis methodologies but are waiting on QP approval of their manufacturing method.
- The following SMEs have or are currently building GMP environment: Procella, XNK Therapeutics, Anocca, Xintela and Amniotics.

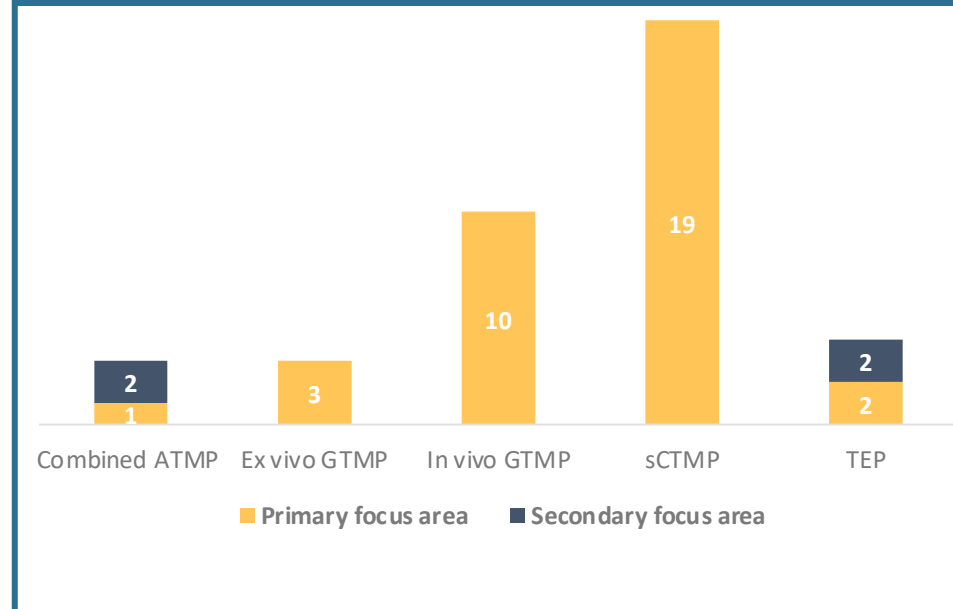
* One company answered that they have both an upcoming partnership as well as a batch already manufactured. In this graph they are only included in "Yes at least one batch is manufactured"

Nordic ATMP expertise is focused on sCTMP therapeutics

ATMP focus area of survey responders (n = 19)

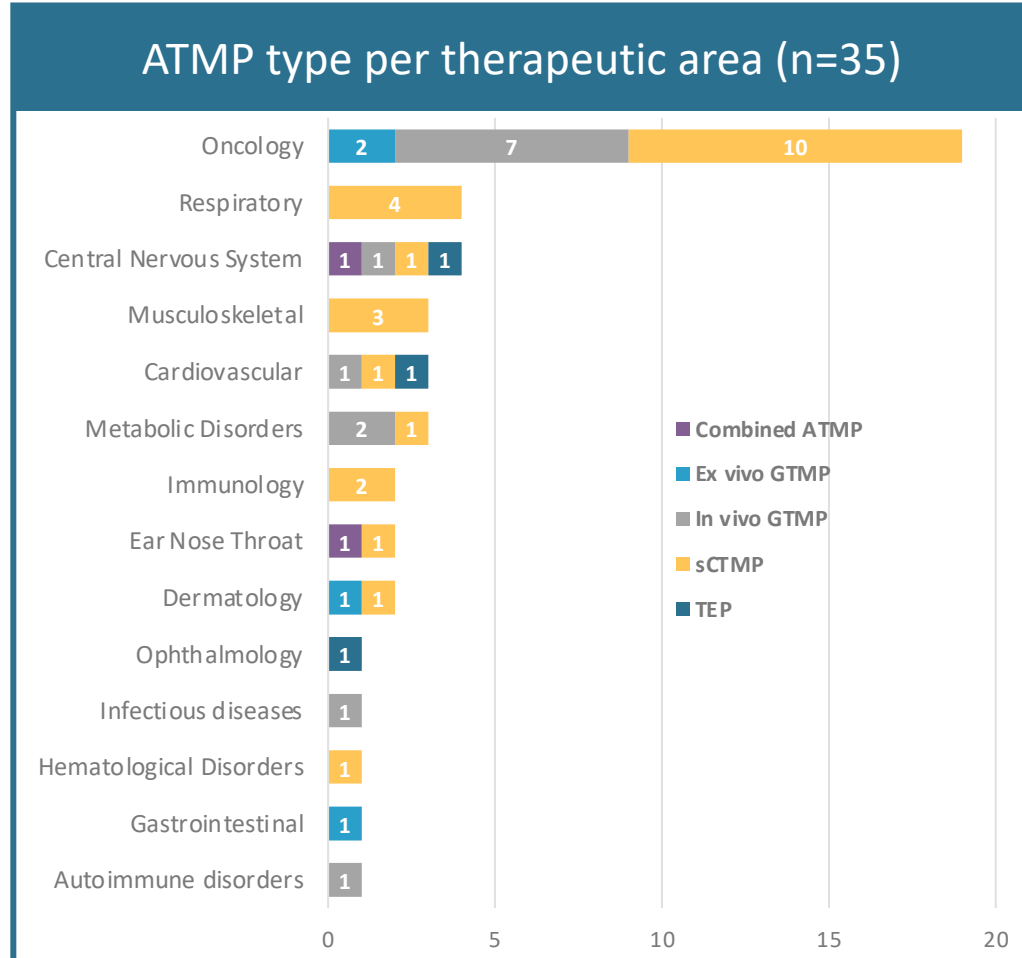


ATMP focus area of all identified SMEs (n=35)



- The main focus area of ATMP companies is determined based on their lead programs and research focus. If a company reported several focus areas in the ATMP survey, we have judged which one is their main area and which is secondary based on what their lead program is.
- Most biotech companies only have one focus area, and for those that have more, the most common secondary activity is combined ATMPs and TEPs.
- It is rare to have combined ATMPs as the main focus area.

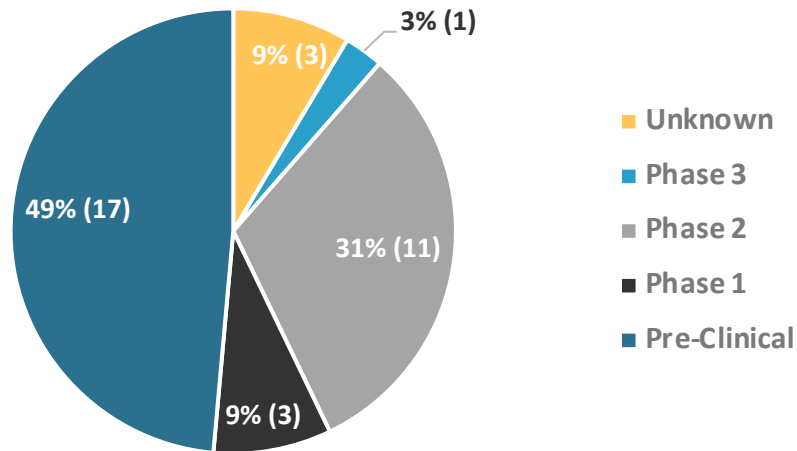
ATMPs target a large set of therapeutic areas



- This graph contains information on which therapeutic areas that companies are active in. Note that a company can be active in more than one therapeutic area.
- Additionally, if a company has more than one program for the same therapeutic area, it is still only counted as one, this is in order to look at company level and not by project level.
- The graph contains information from all 34 identified companies.
- The by far most common indication is oncology, with 19 active companies.
- Apart from oncology the field is very varied, with maximum four companies active in any therapeutic area.
- The wide spread of therapeutic areas is indicative of that ATMPs in the future will target a wide set of diseases.

49% of the identified companies have their most mature asset in pre-clinical development

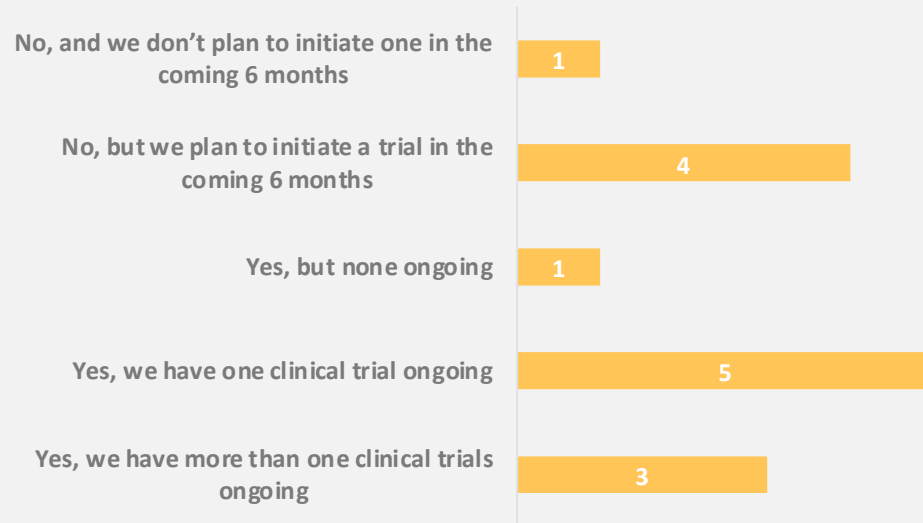
Latest stage asset of all identified SMEs (n=35)



- The Nordic industry is in general still in an early phase. There is only one company in Phase 3.
- The data is based on the information on the companies' websites. There they often refer to assets as Phase 2, though it is reported as Phase 1/2 in ClinicalTrials.gov.

All GMP active companies, but one, have initiated, or plan to initiate clinical trials

Clinical trial development of GMP active* companies (n=14)



- There is only one company with GMP activity that does not have plans to initiate trials in the upcoming 6 months.
- Of the 4 trials upcoming in the next 6 months, none have a NCT number yet.
- Of the companies that responded that they have more than one ongoing trial, two companies have three ongoing trials, and one have two ongoing trials.

* Includes companies that either have their own GMP production or companies that have a GMP partner.

A total of 18 Nordic SME ATMP trials are either ongoing or planned

Clinical trial number	Phase	Start year	Location	Number of Nordic patients included in trial	Status
NCT02749331	Phase 1/2	2016	Uppsala, Sweden	7	Recruiting
NCT02705196	Phase 1/2	2016	US	0	Recruiting
NCT03225989	Phase 1/2	2018	Sweden	50	Recruiting
NCT03973827	Phase 1/2	2019	Huddinge, Sweden	15	Active, not recruiting
NCT04123470	Phase 1/2	2020	US/Uppsala, Sweden	n/a	Recruiting
NCT04447833	Phase 1	2020	Uppsala, Sweden	7	Active, not recruiting
NCT04896853	Phase 1	2021	Örebro, Sweden	9	Recruiting
NCT04869397	Phase 2	2021	Montreal, Canada	0	Recruiting
NCT05061030	Phase 1/2	2021	Uppsala, Sweden	66	Not yet recruiting
NCT03784131	Phase 1	2021	Spain	0	Not yet recruiting
NCT04558931	Phase 2	2021	Huddinge, Sweden	n/a	Recruiting
NCT05277350	Phase 1	2022	US	0	Not yet recruiting
EudraCT 2019-000680-24	Phase 1	2019	Uppsala	192	Ongoing
EudraCT 2021-000563-69	Phase 2	2021	n/a	n/a	Ongoing
n/a		Next 6 months	Uppsala, Sweden	18	Not active yet
n/a		Next 6 months	n/a	n/a	Not active yet
n/a		Next 6 months	Australia	0	Not active yet
n/a		Next 6 months	Sweden	12	Not active yet

- Good to know: We did not include the company names here, since we said that no data would be connected to them as a company.
- It is common for Nordic companies conduct trials abroad, especially in the US.
- The two most productive companies are conducting three trials each.
- Sweden is the only Nordic country where Nordic SMEs have trial locations, suggesting that Sweden is the most mature country in terms of accessibility to support functions related to clinical trials.
- In Sweden the trials are centered around the Karolinska and Uppsala University Hospitals.

* The data on the number of Nordic patients comes from the survey. If it was not specified in the survey, it is left as n/a, except if the trial is only conducted in the nordic region, then the number of estimated patients on ClinicalTrials.gov was used.

Focus on international pharmas

International companies answering the survey

- There are international companies conducting ATMP research in the Nordic region, though the extent is unknown as only answers from six pharma companies were received.
- Of these six, four companies were included in the analysis, and two companies, CellSeed and Chiesi were excluded due to not having any ATMP activity in the Nordic region.
- The four companies that were selected are all large pharmaceutical companies located in Stockholm, except AstraZeneca that is in Gothenburg.

Respondants included in results

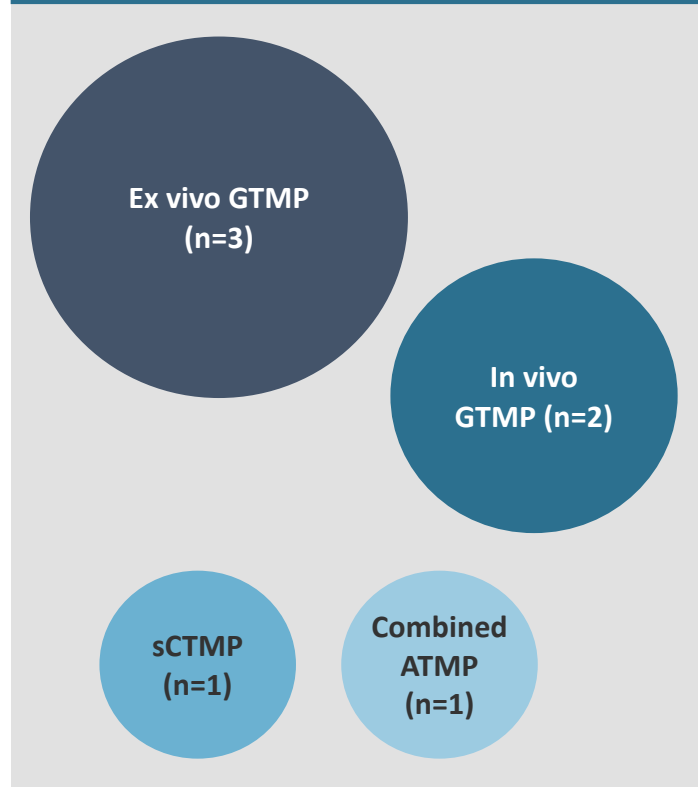


Respondants excluded from results



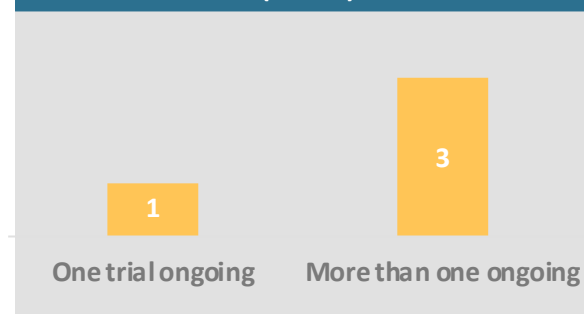
Large pharmaceutical companies are predominantly active in ex vivo GTMP

ATMP focus areas* of Big Pharmas active in Sweden (n = 4)



*Note that a company can have multiple focus areas

ATMP trials ongoing (n=4)



- GTMP, and especially ex vivo gene therapy is the main focus area of the large pharmaceutical companies that responded to the survey.
- One common ex vivo GTMP type is CART. The most advanced trial is in Phase 3, but there are also approved CAR-T products such as Kymriah and Yescarta.
- One company reported that they had four trials on going, one company had two trials ongoing, and the most productive company BMS, had 17 trials ongoing.
- A total of 4 companies had manufactured a batch of any of their products under GMP compliance. The same 4 companies had initiated at least one clinical trial.

Sources: MSC analysis based on ATMP survey

At least eight pharma trials include Nordic study sites

Trial number	Phase	Start year	Location	Number of Nordic patients included in trial*	Status
NCT03484702	Phase 2	2018	EU, Asia	5	Active, not recruiting
NCT04245839	Phase 2	2020	US, CAN, EU, Asia	5	Recruiting
NCT03435796	Phase 2/3	2018	US, CAN, EU, Asia	10	Recruiting
NCT04181827	Phase 3	2020	US, Asia, AU, EU	10	Active, not recruiting
NCT04923893	Phase 3	2021	WW, excl Africa	10-20	Recruiting
NCT03651128	Phase 3	2018	US, CAN, EU, Asia	5-10	Recruiting
NCT03575351	Phase 3	2018	US, EU, Asia	5-7	Active, not recruiting
NCT03861273	Phase 3	2019	WW, excl Africa	n/a	Active, not recruiting

- There are 23 trials conducted by the pharmas active in ATMP in Sweden, of these at least 8 include Nordic patients with a total amount of ~60 included patients.
- The trial with n/a has not disclosed how many Nordic patients the aim to include, but the trial includes study sites in Skåne.
- It is unclear whether all reported trials stem from ATMP research conducted in the Nordic region.
- The Janssen CARTITUDE-5 trial has study sites in Gothenburg, Stockholm, Linköping, Skåne and Uppsala, making it the trial that is conducted in the most Nordic locations.
- The most popular Swedish trial site is Karolinska, where 5 trials are ongoing.
- Skåne university hospital is the only site in Sweden where the Pfizer hemophilia trial is being conducted.

* The data on the number of Nordic patients comes from the survey

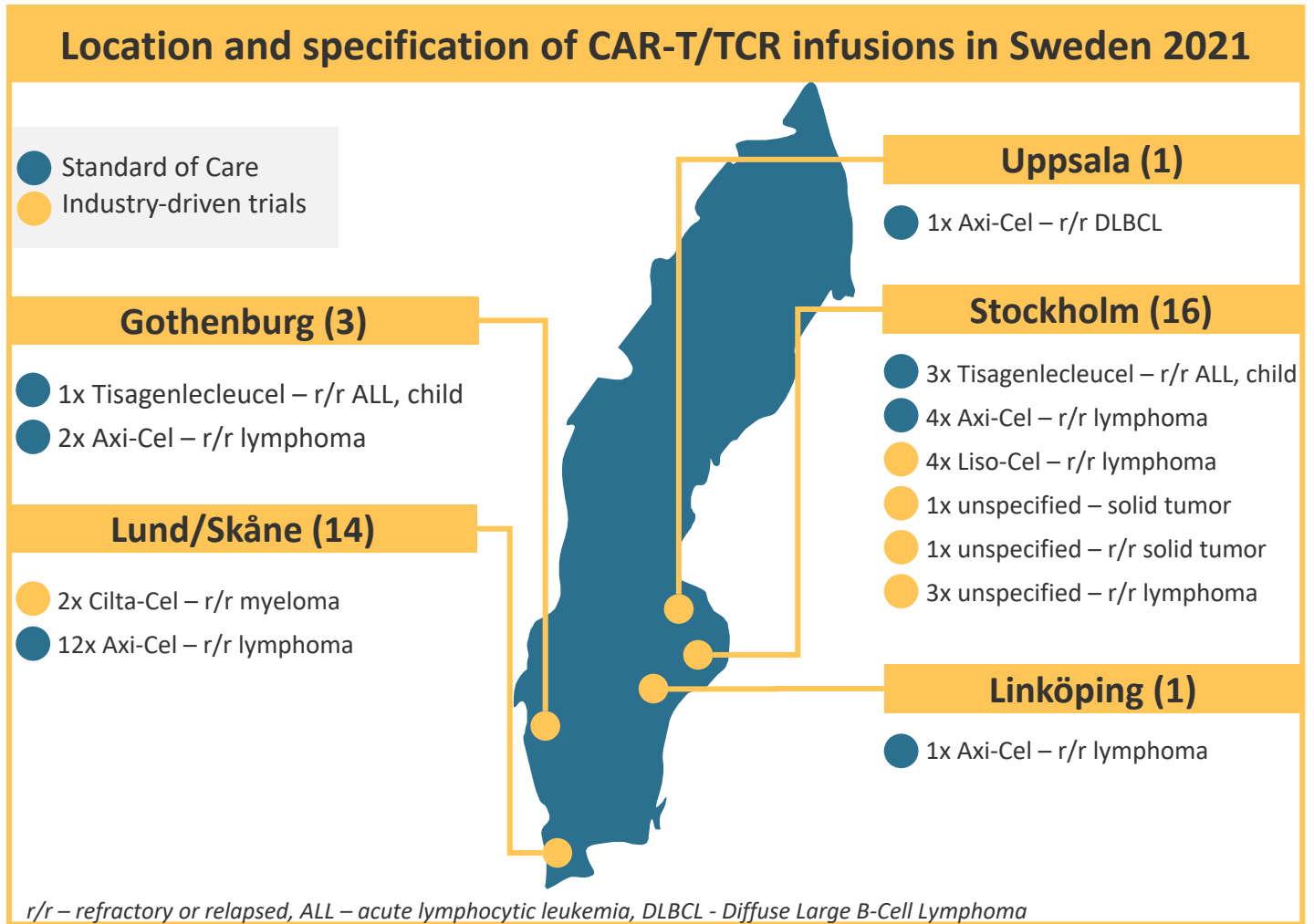
There are 14 active Pharma trials reported with no Nordic patients included

Trial number	Phase	Start year	Location	Status
NCT02631044	Phase 1	2016	US	Recruiting
NCT03310619	Phase 1/2	2017	US	Recruiting
NCT03331198	Phase 1/2	2017	US	Recruiting
NCT03361748	Phase 2	2017	US, CAN, EU, Asia	Active, not recruiting
NCT03548207	Phase 1/2	2018	US, Asia	Active, not recruiting
NCT03744676	Phase 2	2018	US	Active, not recruiting
NCT03483103	Phase 2	2018	US	Active, not recruiting
NCT03743246	Phase 1/2	2018	US, EU	Recruiting
NCT03601078	Phase 2	2018	US,EU	Recruiting
NCT04133636	Phase 2	2019	US, EU	Recruiting
NCT04231747	Phase 1/2	2020	US	Recruiting
NCT04196491	Phase 1	2020	US	Active, not recruiting
NCT04394650	Phase 1	2020	US	Recruiting
NCT04855136	Phase 1/2	2021	US,EU	Recruiting

Focus on CAR-T infusions in Sweden 2021

Lund and Stockholm hospitals are the only ones doing CAR-T trials in Sweden

- There are 5 university hospitals that specified that they used CAR-T/TCR* infusions during 2021.
- The only approved therapies in use in Sweden are Tisagenlecleucel and Axi-Cel for leukemia and lymphoma respectively.
- Cilta-Cel (Janssen) and Liso-Cel (Bristol-Myers Squibb) are currently tested in Phase 3 trials.
- There are 5 trials for solid tumors and lymphoma where the product is not specified.

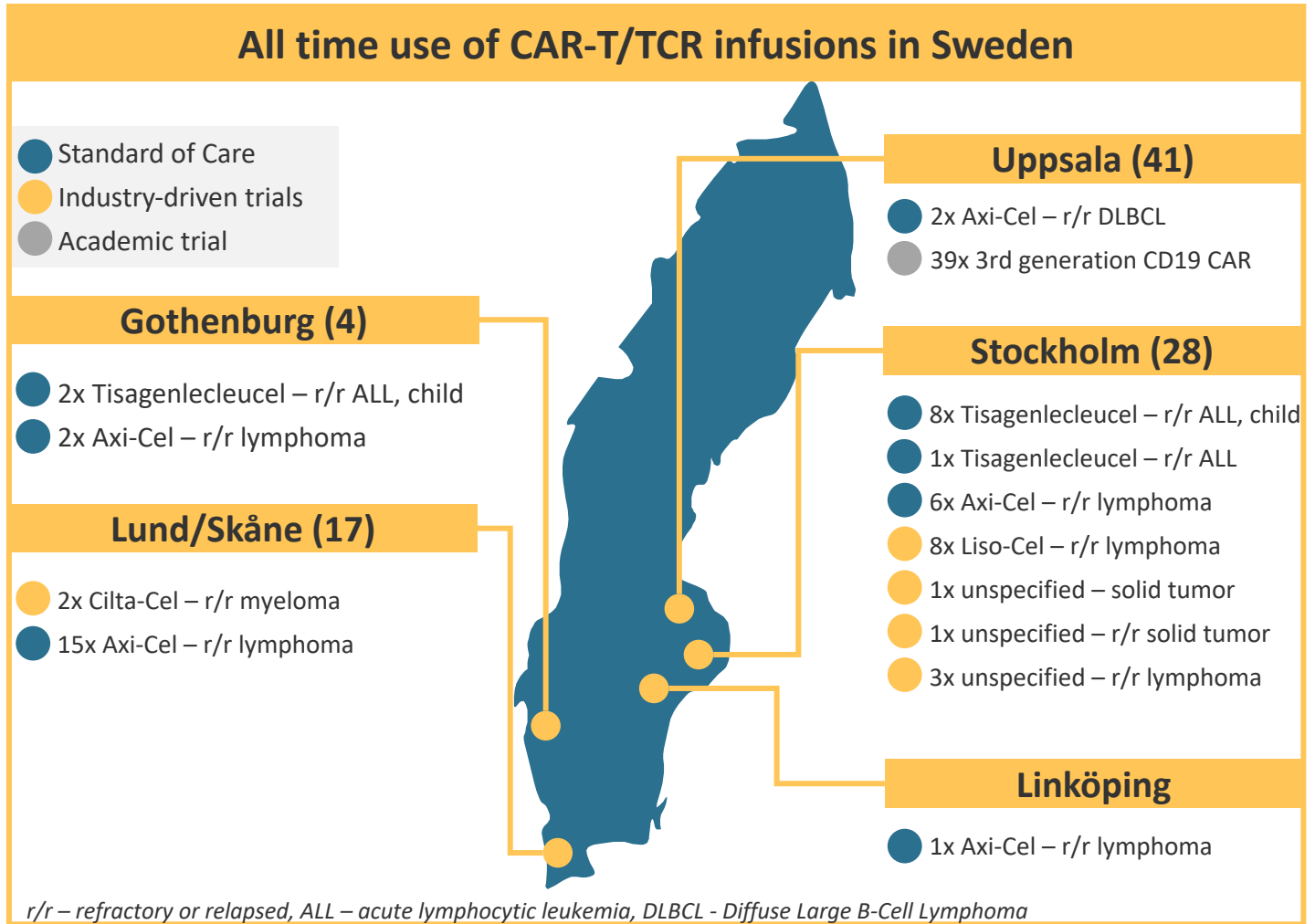


* Chimeric antigen receptor T-Cell / T-Cell Receptor engineering

Sources: MSC analysis based on ATMP survey

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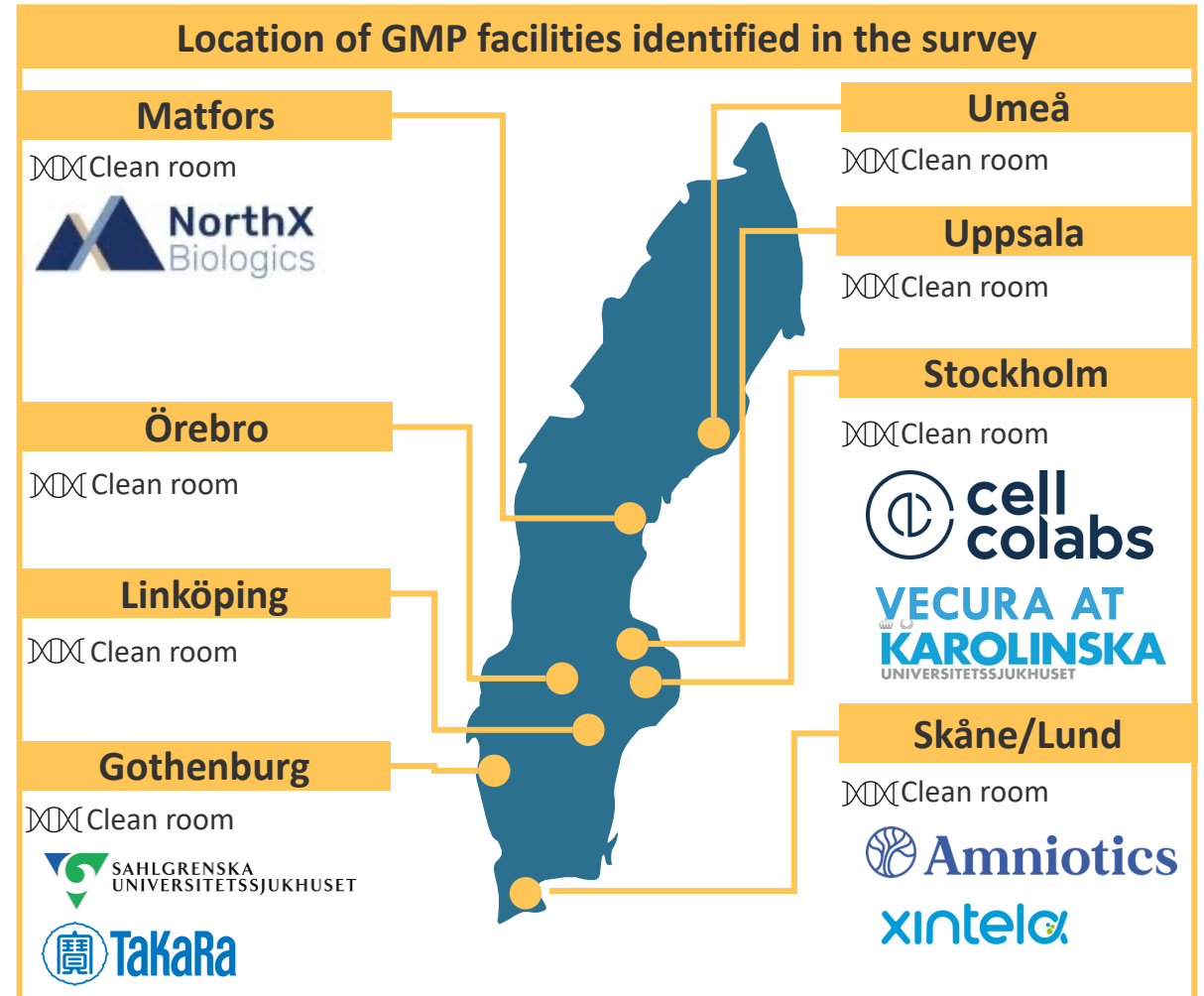
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Sources: MSC analysis based on ATMP survey

Facilities for GMP manufacture

Six GMP facilities in Sweden have been identified in the survey

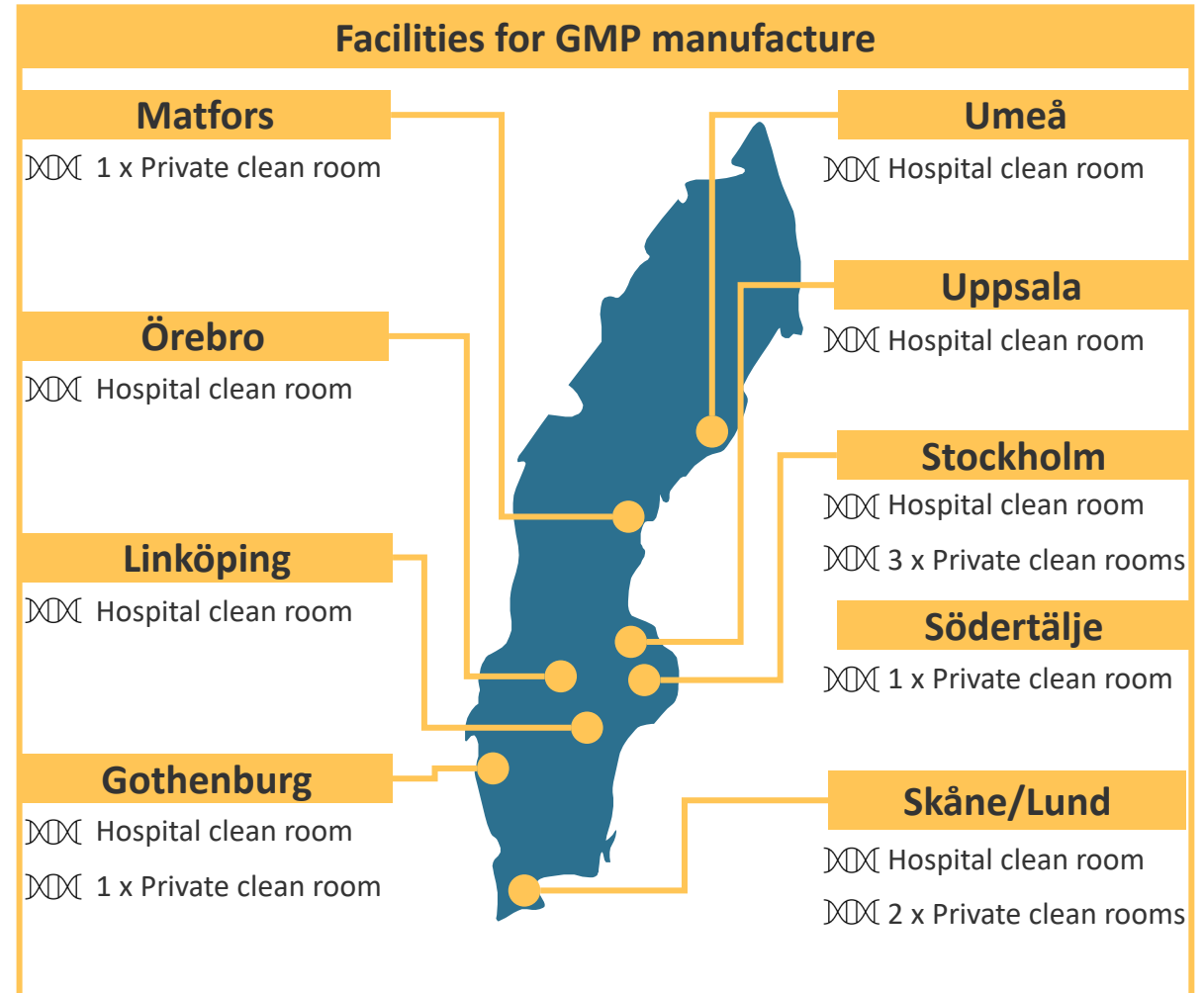
- This is a map of GMP facilities in Sweden. Six of these were identified in the survey and are marked with their respective logos.
- The general clean room means that there are cleanrooms for manufacture located in the city, though not identified in this survey.



Sources: MSC analysis based on ATMP survey and ATMP Sweden ([link](#))

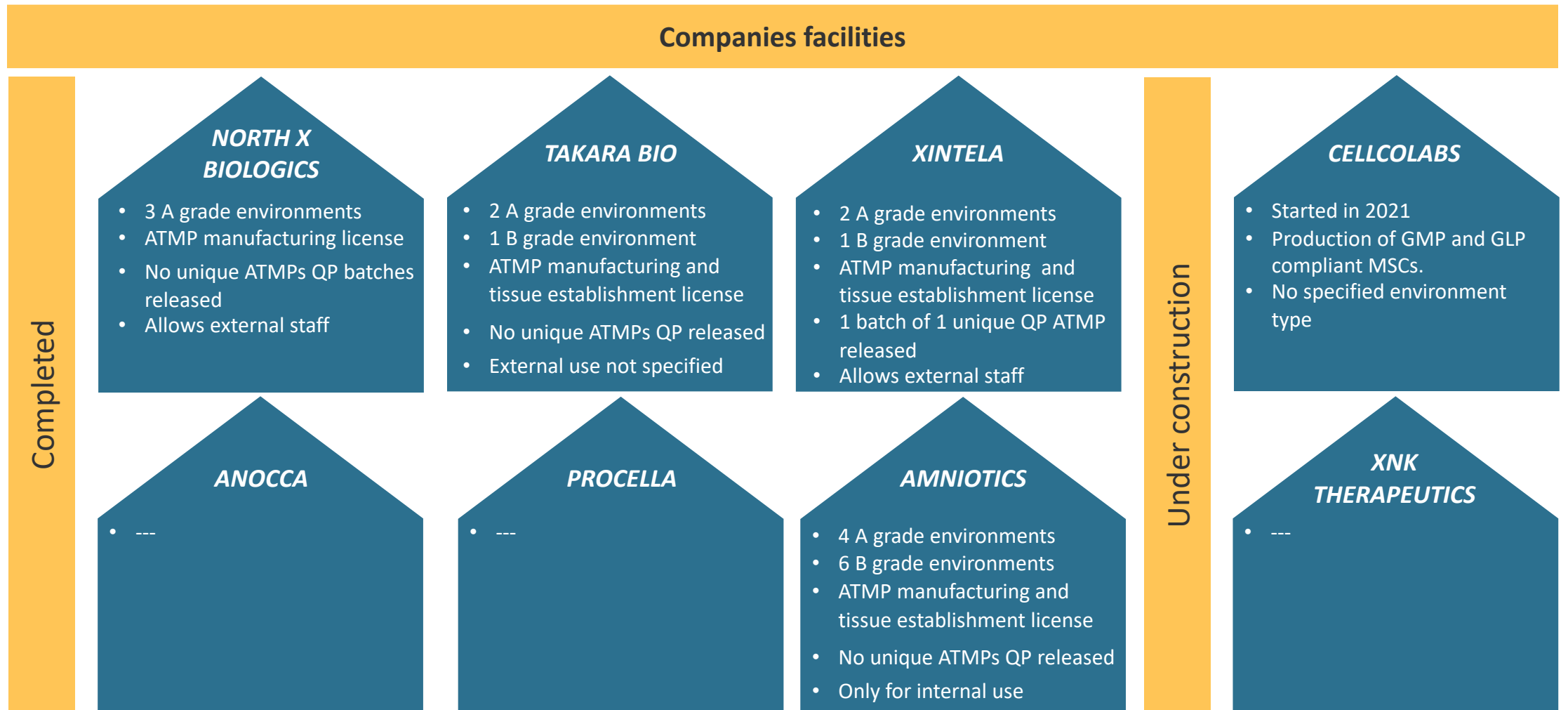
Six GMP facilities in Sweden have been identified in the survey

- This is a map of GMP facilities in Sweden.
- There are both private clean rooms owned by companies and clean rooms located at hospitals.
- Note that not all sites are completed and approved for GMP manufacture.



Sources: MSC analysis based on ATMP survey and ATMP Sweden ([link](#))

Commercial actors with GMP environments



University/hospital actors with GMP environments

University hospital associated clean rooms

Completed

SAHLGRENSKA UNIVERSITY HOSPITAL

- 1 B grade environments
- ATMP manufacturing and tissue establishment license
- 500 batches of 3 unique QP ATMPs released
- Only for internal use

VECURA AT KAROLINSKA

- 9 A grade environments
- 1 B, 3 C grade environments
- ATMP manufacturing and tissue establishment license
- Multiple ATMPs QP batches released
- Allows external staff

Additional information on slides 28 and 29

Slide 28

- The following SMEs have or are currently building GMP environment: Procella, XNK Therapeutics, Anocca, Xintela and Amniotics.
- Cellcolabs is on the Karolinska Solna Campus, but it is privately owned by Takura and Norrsken foundation.
- NorthXBiologics and Takura are service providers who support companies related to the production of ATMPs and have their own GMP-sites.

Slide 29

- Vecura, located at the Karolinska University Hospital in Huddinge, is owned by the Karolinska Cancer Centrum (KCC).
- The department of Clinical Immunology and Transfusion Medicine at Sahlgrenska University Hospital also have a GMP facility.



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