Nordic ATMP landscape and implications for the scale of an infrastructure for process development and manufacturing

Visionsdriven hälsa

March 2021

MSC | STRATEGY & COMMUNICATION

MSC Nordics empowers biotech companies to attract investments and strike strategic partnerships.

MSC STRATEGY & COMMUNICATION

Disclaimer

This report has been prepared by M S&C Nordics AB ("MSC") for the Vinnova funded project 'Visionsdriven hälsa'. All information contained in this report and any other documents provided by MSC are subject to this legal notice.

This report includes certain market analyses, provided for general use purposes only. It may not be applicable or appropriate in all situations. MSC makes no representation or warranty, express or implied, as to the accuracy or completeness of the information contained in this report that is, or that is based on, the information or data provided by the interview subjects or any third-party (including any assumptions incorporated therein or any projections, estimates, conclusions or opinions generated thereby).

MSC is not able to predict future events, developments and uncertainties. Consequently, any of the prediction or forecast statements contained in this report may prove to be incorrect or incomplete, and actual results could differ from those projected or estimated in this report. MSC undertakes no obligation to update any forward-looking statements for revisions or changes after the date of this report and MSC makes no representation or warranty that any of the projections or estimates in this report will be realized. Nothing contained herein is, or should be relied upon as, a promise or representation as to the future.

MSC is not responsible for any suffered damages arising from decisions based on this report and or any made future predictions, except to the extent it is determined by applicable mandatory law.

Table of content

List of abbreviations

ATMP – Advanced Therapeutic Medicinal Product

GTMP – Gene Therapy Medicinal Product

CTMP – Cell Therapy Medicinal Product

GM CTMP – Gene Modified Cell Therapy Medicinal Product

TEP – Tissue Engineered Products

GMP – Good Manufacturing Practice

CAGR – Compound Annual Growth Rate

MeSH – Medical Subject Headings

Executive Summary

A project analyzing Nordic ATMP landscape and future manufacturing needs of a ATMP infrastructure organization

- The aim of this report is to present an independent analysis of the current Advanced Therapeutic Medicinal Product (ATMP) landscape in the Nordics and estimate the projected scale of a Nordic ATMP infrastructure organization.
- The purpose of the analysis is to spread knowledge around the Nordic ATMP market, as well as support the Vinnova funded project 'Visionsdriven hälsa' in the development of an ATMP infrastructure organization with capabilities, amongst other, in manufacturing.
- The analysis was based on secondary research by publications and proprietary software as well as primary research by interviews with industry leaders, similar infrastructure organizations and Nordic ATMP companies.

LANDSCAPE ANALYSIS OF THE CURRENT ATMP LANDSCAPE

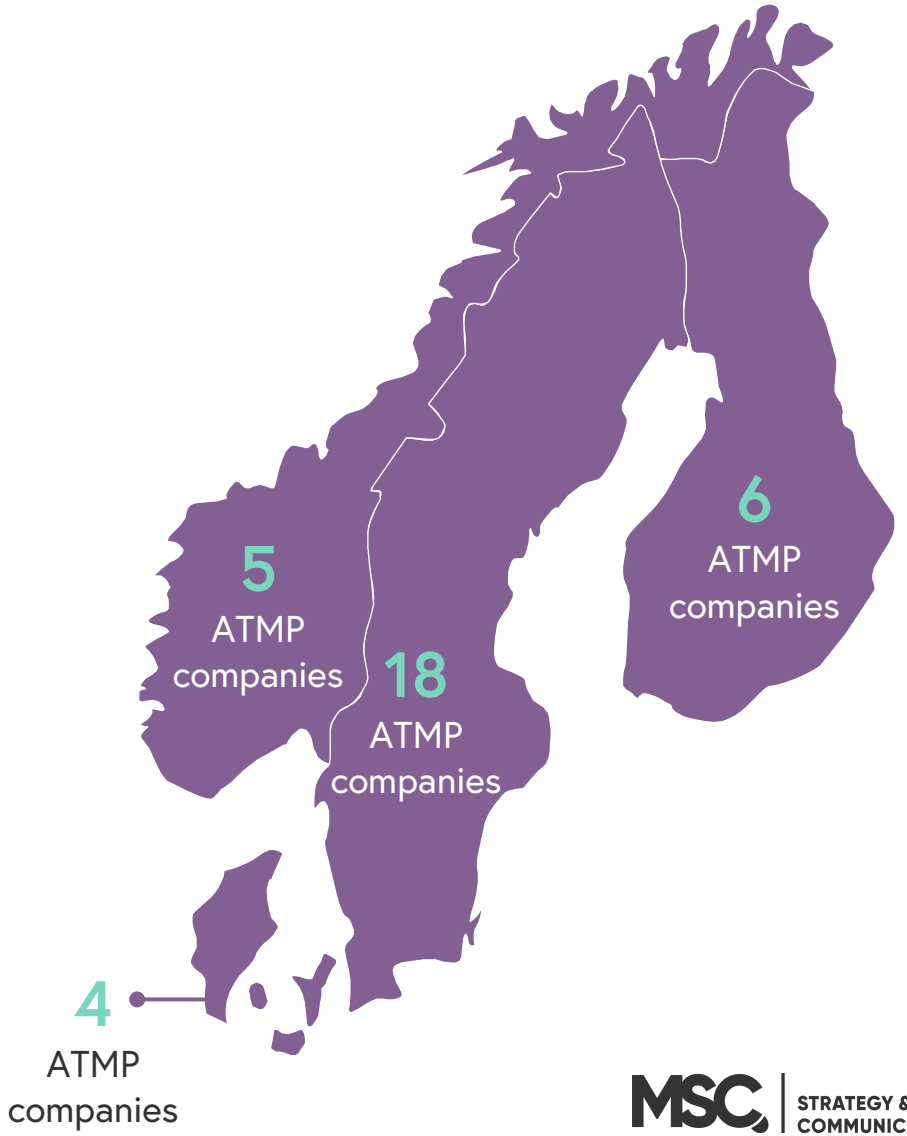
- **Mapping Nordic countries' (Sweden, Denmark, Norway and Finland) ATMP companies, projects, research groups, publications and big pharmaceutical companies with ATMP efforts within the country.**

PROJECTED SCALE OF A NORDIC INFRASTRUCTURE FOR ATMP

- **Projection of number of companies expected in the Nordics in each phase, until 2030.**
- **Projection of how many projects an ATMP infrastructure can capture, and how many clean rooms of each type is needed.**

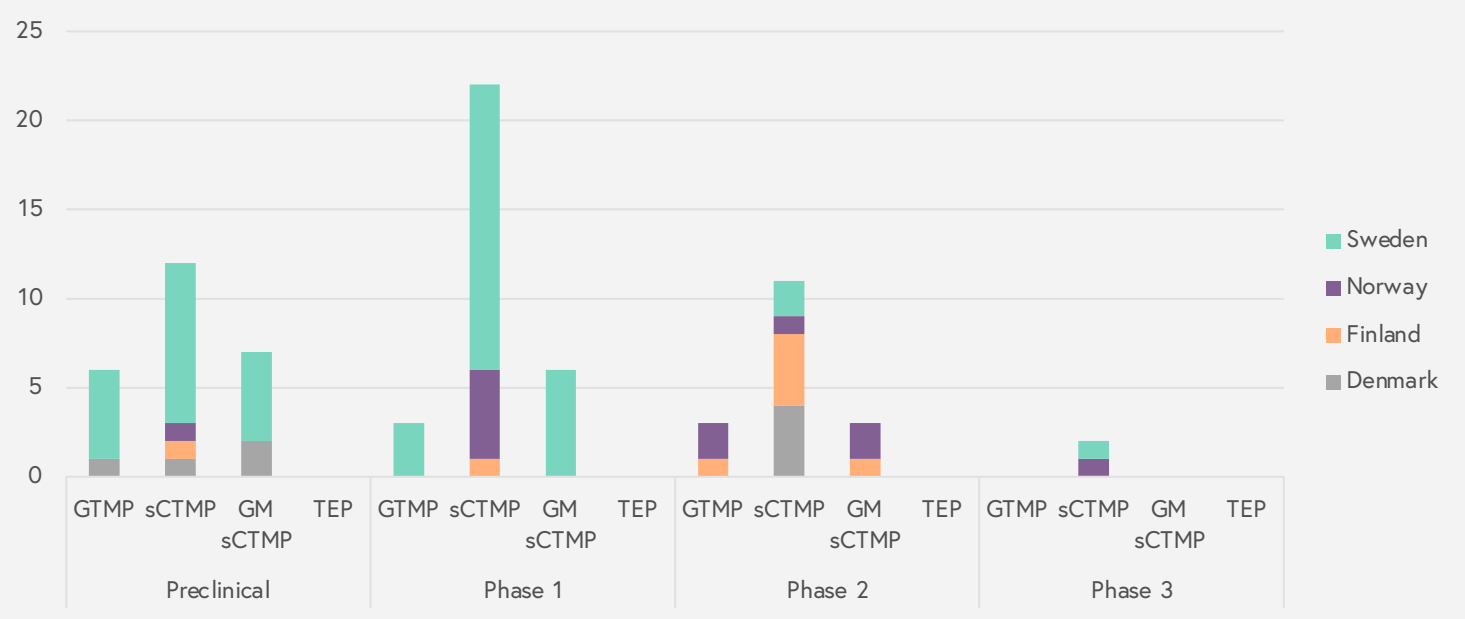
Executive summary

- The analysis of Nordic ATMP companies show that there is an even distribution in companies developing cell therapies (CTMPs), gene therapies (GTMPs) and gene modified cell therapies (GM CTMPs), with a total of 33 ATMP companies.
- Since Denmark, Norway and Finland hold fewer companies than Sweden (also per capita), it could be so that a higher growth will be seen in these countries in the years to come.
- Oncology is the largest indication area that Nordic ATMP companies focus on, accounting for the majority of projects in all countries.
- The ATMP field is in its infancy and this is reflected by most companies being in early development phases.
- The ATMP field is expected to experience rapid growth in the coming years and is estimated to increase to nearly 80 companies in 2030 (compared to 33 at year end 2020).
- ATMP related projects in Nordic companies are expected to increase from 75 to 174 from 2020 to 2030.
- Based on a market share of 20%, a new ATMP organization with production capabilities would need 18 clean rooms by 2030 to fulfill the needs of the Nordic ATMP market.



MSC | STRATEGY & COMMUNICATION

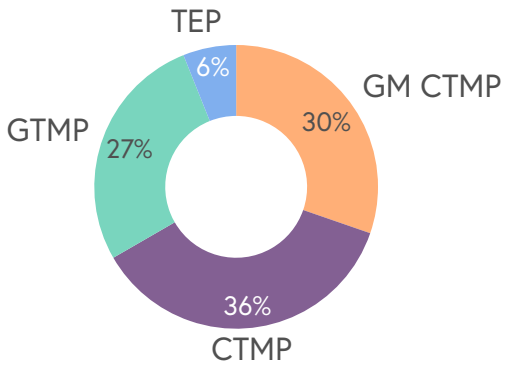
Executive summary



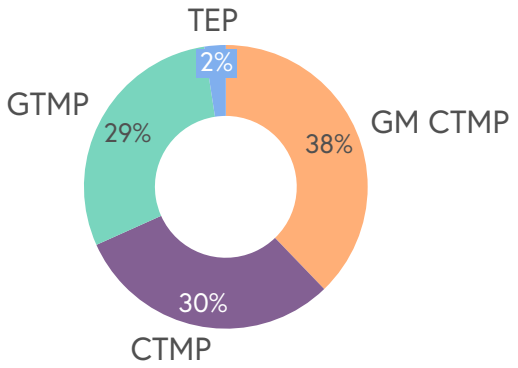
ATMP development programs in the Nordics

- CTMPs, GTMPs and GM CTMPs account for about 94% of the 33 ATMP companies in the Nordics, while Tissue Engineered Product (TEP) companies are only constituting about 6% of the 33 companies.
- Sweden is the dominating country, in terms of number of companies and number of development programs. However, Sweden is lagging behind Denmark in the number of research groups active in the ATMP field.

Distribution of Nordic ATMP companies



Distribution of Nordic ATMP projects



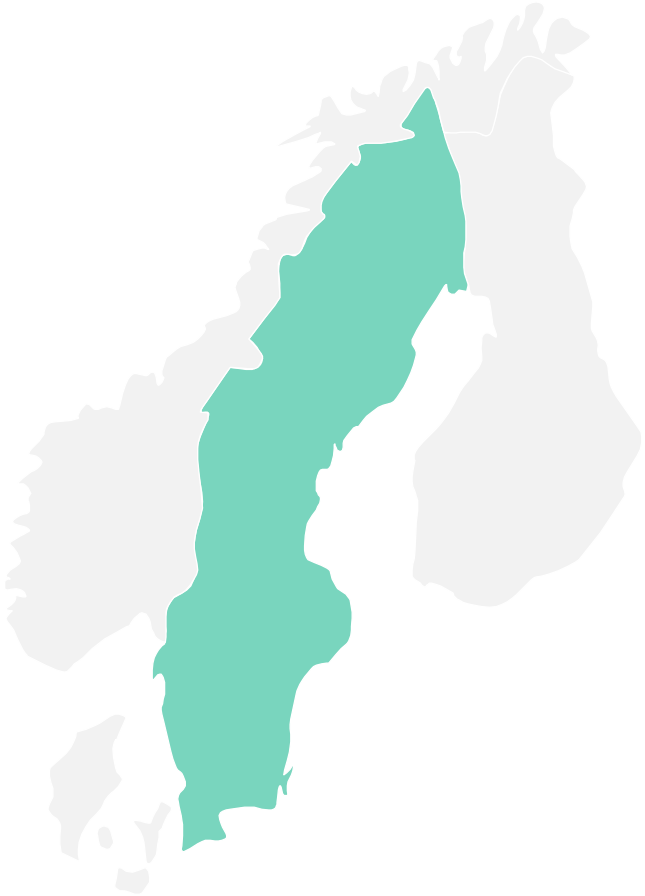
NOTE: Data was retrieved continuously during Q4 in 2020 and, as such, might not be exhaustive and could have changed over time.

MSC STRATEGY & COMMUNICATION

Landscape analysis

SWEDEN

Sweden is the most active country within ATMPs in the Nordics, regarding the amount of research output and companies



A summary of the ATMP field in Sweden

- There are 18 national companies developing therapies in ATMPs.
- Within those 18 companies, there are 46 development programs ongoing where most of these programs were identified as being in early development stages.
- The most abundant type of project is GM CTMPs (25), followed by CTMP projects (19).
- Almost 40% of all programs are being developed by two companies (Immunicum and Lokon Pharma).
- Published ATMP related research from Swedish affiliations vary between 30 and 65 publications per year.
- 17 research groups were identified as being focused on ATMP research.
- In addition to the above, there are 3 international companies that have shown signs of ATMP development in Sweden.

There are currently 18 SME companies with therapeutic ATMP R&D activity in Sweden

The SME companies are defined by being founded and having their main operating activity in Sweden. The maturity level varies, but all have development programs in preclinical or clinical stage.

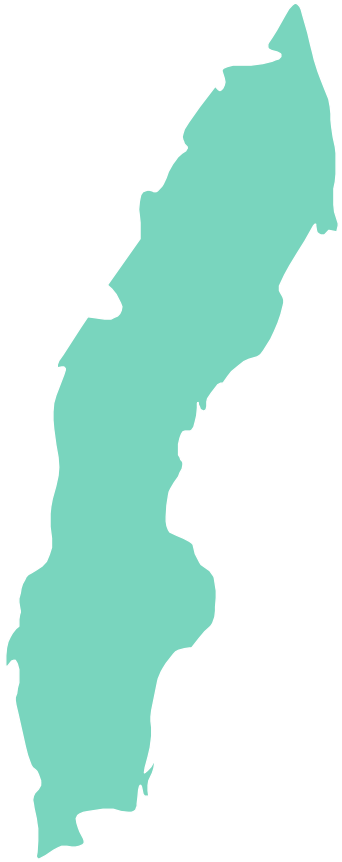
NOTE
CellSeed have a Swedish affiliation set up for conducting clinical trials. They are not included due to their lack of focus and R&D in Sweden. Takura have subsidiaries that have some activity in ATMP.

Source: Nordic Life Science Database, Biomedtracker, ATMP Sweden, MSC analysis, Interviews

3 international companies were identified with ATMP-related R&D activities in Sweden

AstraZeneca

Pfizer



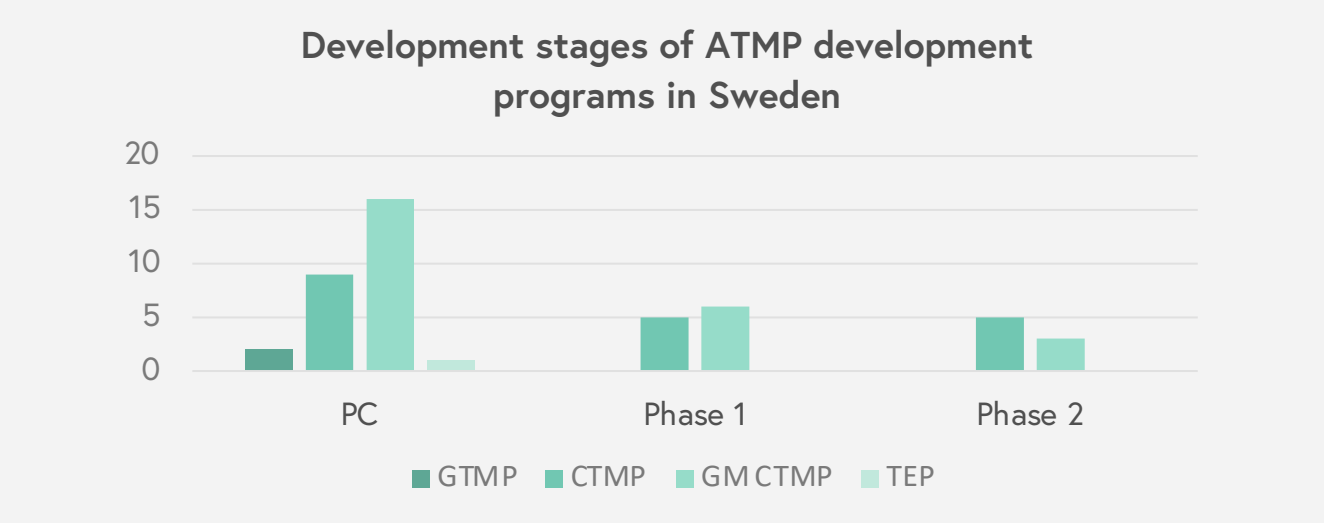
Chiesi

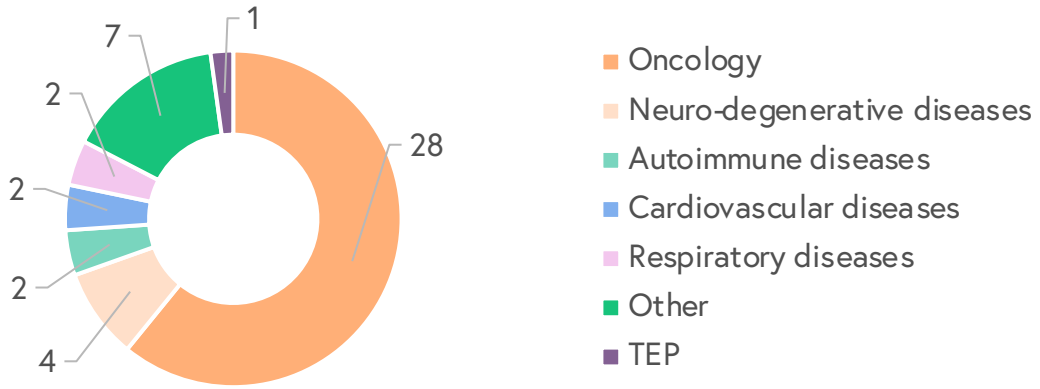
The international companies are defined by being global players as well as having approved products, inhouse production of APIs and ATMP related R&D activities within Sweden*.

Source: Company websites, MSC analysis

*Pfizer has an indirect evidence of ATMP R&D in Sweden, given the biologics production site in Strängnäs.

A majority of the 47 ATMP development programs that are being developed by Swedish SME companies are in preclinical stage





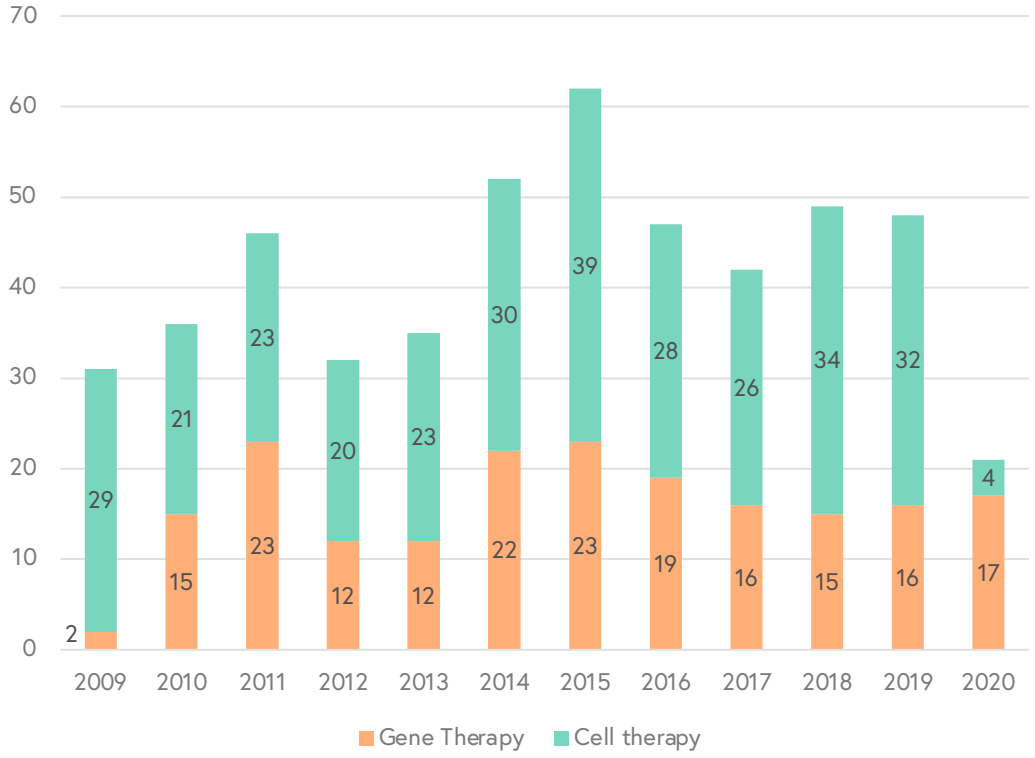
ATMP development programs in Sweden

- A total of 47 ATMP development programs were identified as being in active development by the 18 SME ATMP companies in Sweden.
- Most of these programs were identified as being in early development stages.
- Oncology is the indication area with the highest concentration of programs.
- Almost 40% of all programs are being developed by two companies (Immunicum and Lokon Pharma).
- Five companies (Nextcell, Immunicum, Lokon Pharma, XNK Therapeutics and Ilya Pharma) are currently in clinical Phase 2.

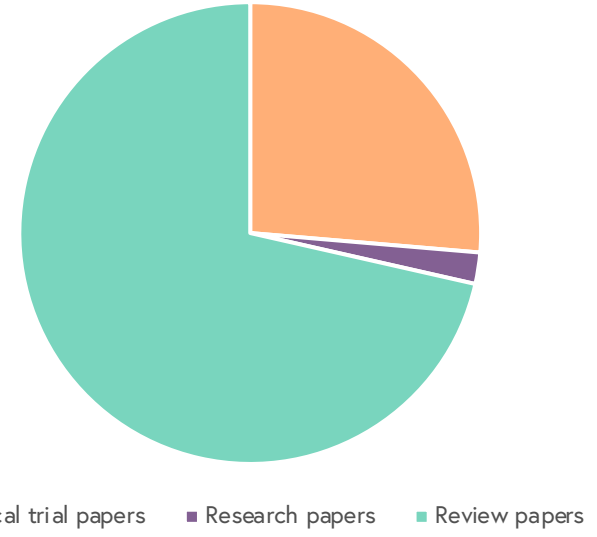
Source: Nordic Life Science Database, Medtrack, ATMP Sweden, MSC analysis

The number of ATMP related publications from Swedish affiliations vary between 30 and 65 per year

Number of ATMP related publications, from Swedish affiliations (2009-2020)*



Publications 2009-2019 divided on publication type



- 2549 publications related to ATMP have been published between 2009-2019.
- Among these, 102 papers have been categorized as relating to clinical trials.

* PubMed indexing for MeSH terms typically is lagging (~6-9 months). The data for 2019 should therefore not be interpreted as the complete dataset.

NOTE
The publications have at least one author connected to a Swedish university, also called affiliation.

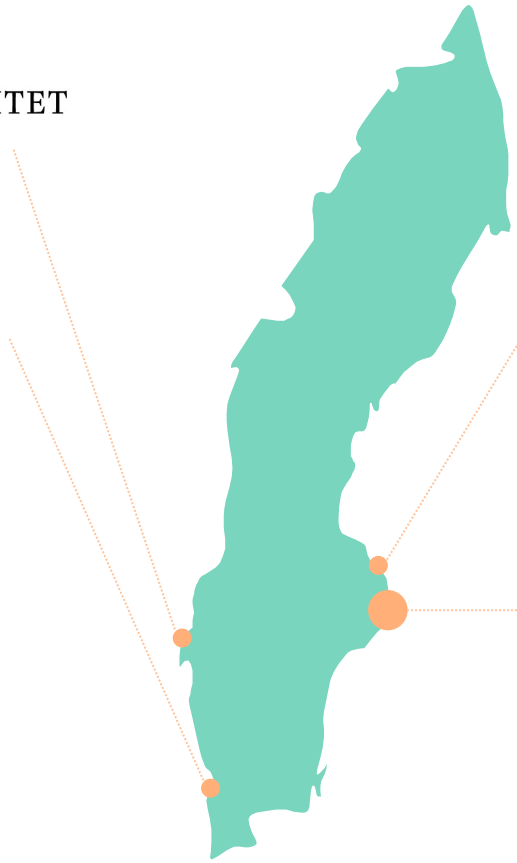
Source: PubMed (see appendix for methodology), MSC analysis

MSC STRATEGY & COMMUNICATION

24 relevant research groups focusing on ATMP research were identified in Sweden

GÖTEBORGS UNIVERSITET
4 research groups

LUND UNIVERSITY
4 research groups



UPPSALA UNIVERSITET
4 research groups

Karolinska Institutet
(Stockholm)
9 Research groups

Other renowned universities with research groups

CHALMERS UNIVERSITY OF TECHNOLOGY
1 research group

KUNGL TEKNISKA HÖGSKOLAN
(Stockholm)
2 Research group

Top Swedish affiliations

BASED ON THE HIGHEST NUMBER OF RESEARCHERS

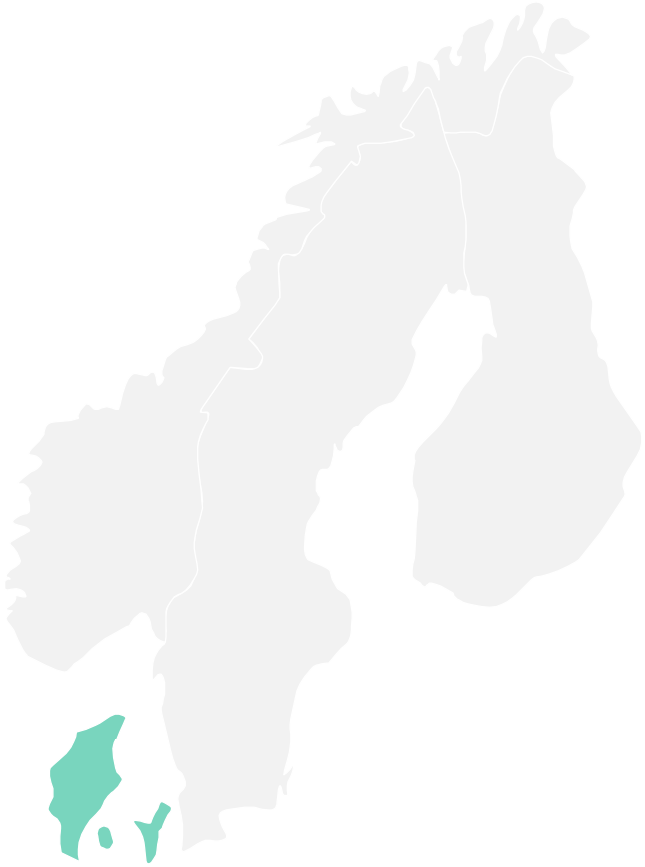
- Karolinska Institutet
- Uppsala University
- Lund University
- University of Gothenburg

The following criteria defined a relevant research group: Having active research within therapeutic applications in ATMP (analyzed by publications), being active at one of the top three universities when ranking by number of publications in ATMP. Top four included due to similar ranking.

Source: Monocl Professional (www.monocl.com, database accessed on Nov-Dec 2020, full methodology in Appendix), MSC analysis

DENMARK

Denmark holds the least amount of ATMP companies in the Nordics, but have a substantial amount of research



A summary of the ATMP field in Denmark

- There are 4 national companies developing therapies in ATMPs.
- Within those 4 companies, there are 8 development programs ongoing where most of these programs were identified as being in early development stages.
- There is an equal amount of CTMP and GTMP projects in Denmark.
- A majority of these programs are focused on oncology and autoimmune diseases.
- The number of published ATMP related publications have decreased during the last years in Denmark.
- 31 research groups were identified as being focused on ATMP research.
- In addition to the above, there are 3 International companies that have shown signs of ATMP development in Denmark.

There are currently 4 SME companies with therapeutic ATMP R&D activity in Denmark

Hørsholm

cytovac

Copenhagen

TWELVE.BIO

SNIPRBIOME
A CRISPR COMPANY

PANCRYOS
INSULIN. NATURALLY.

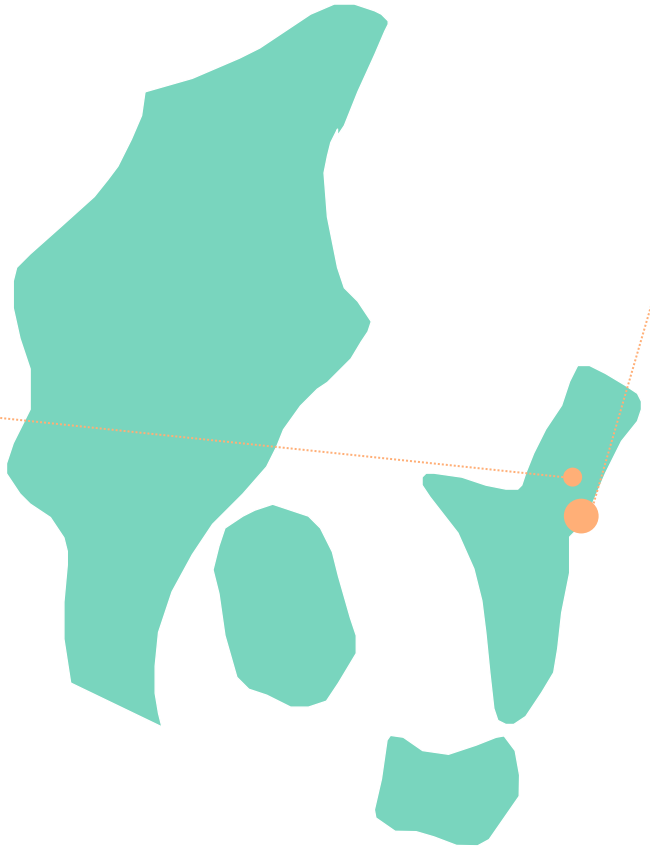
The SME companies are defined by being founded and having their main operating activity in Denmark. The maturity level varies, but all have development programs in preclinical or clinical stage.

Source: Nordic Life Science Database, Biomedtracker, MSC analysis, Interviews

3 international companies were identified with ATMP-related R&D activities in Denmark

Copenhagen

Bagsværd

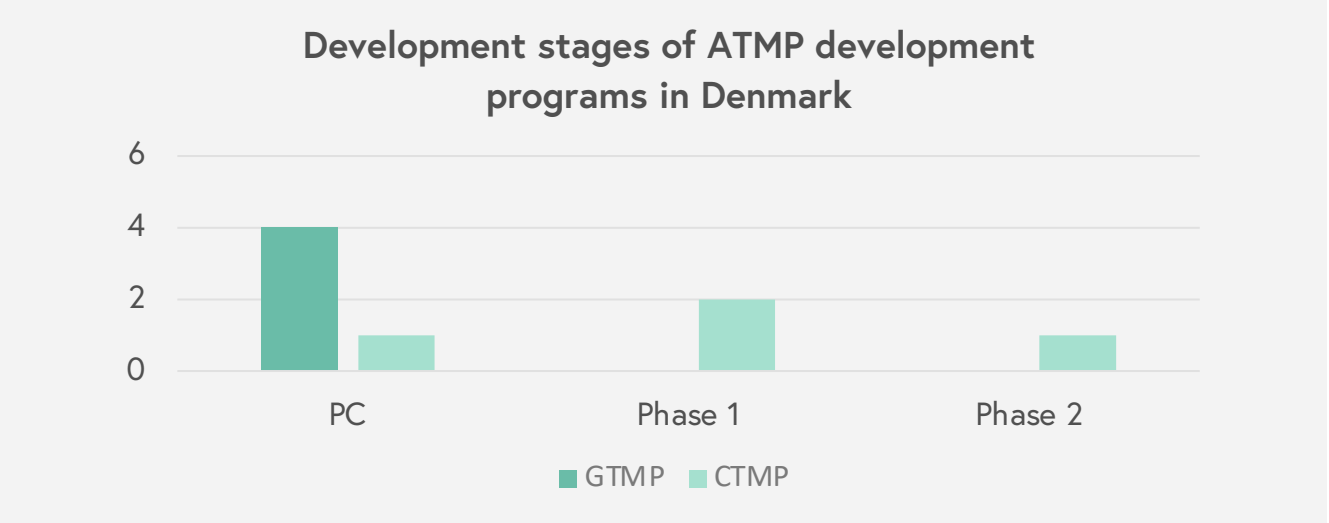


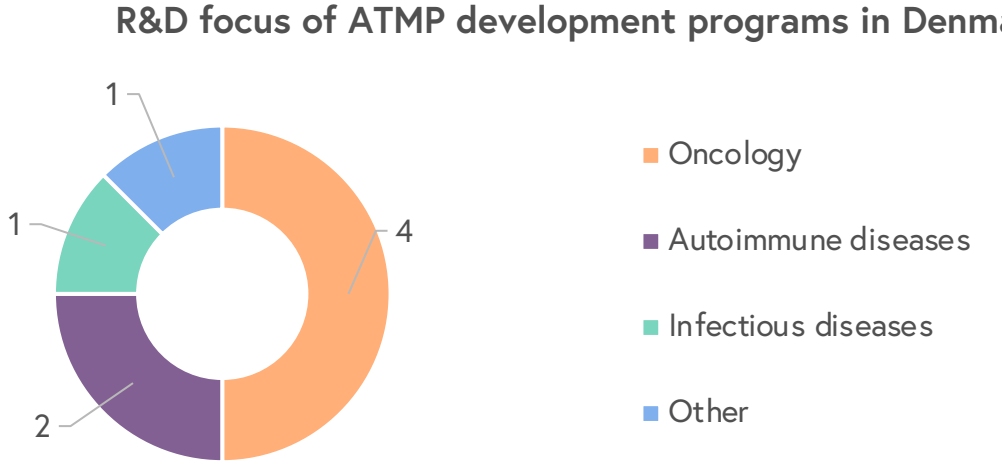
The international companies are defined by being global players as well as having approved products, inhouse production of APIs and ATMP related R&D activities within Denmark*.

Source: Company websites, MSC analysis

*LEO Pharma & Orion Pharma have no disclosed ATMPs in their pipelines, but they have both previously announced collaborations with ATMP research groups.

A majority of the 8 ATMP development programs that are being developed by Danish SME companies are in preclinical stage





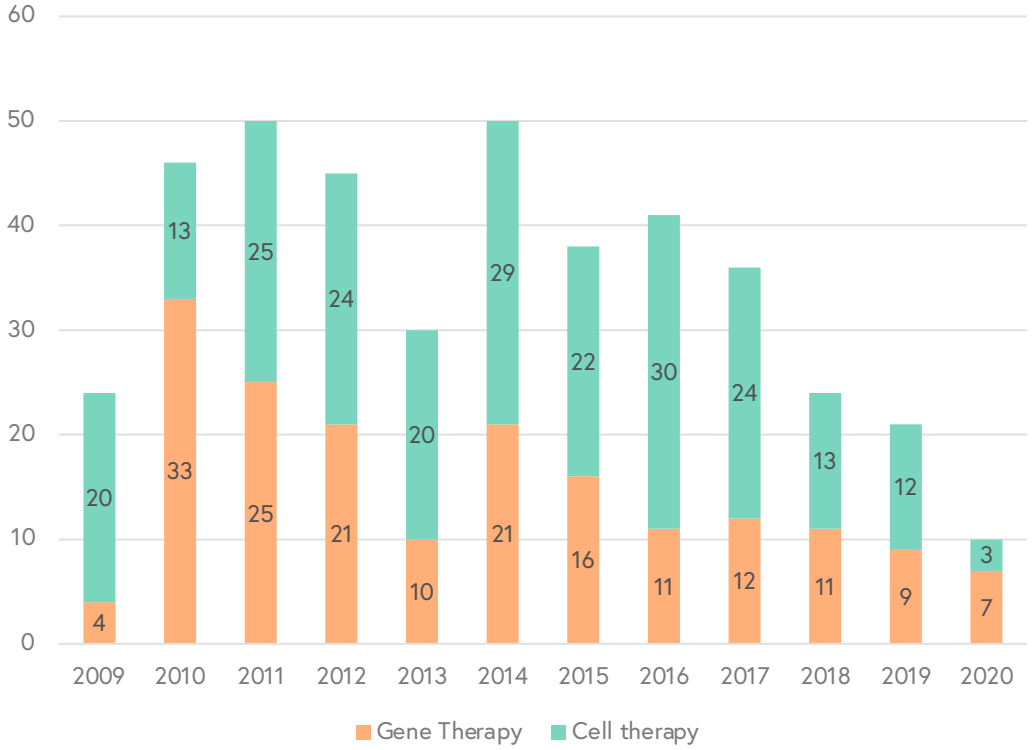
ATMP development programs in Denmark

- A total of 8 ATMP development programs were identified as being in active development by the 4 SME ATMP companies in Denmark.
- Most of these programs were identified as being in early development stages.
- There is about the same number of GTMP programs as CTMP programs.
- A majority of these programs are focused on oncology and autoimmune diseases.
- One active program, an CTMP, is developing a Phase 2 therapy, which is in glioblastoma multiforme (Cytovac).

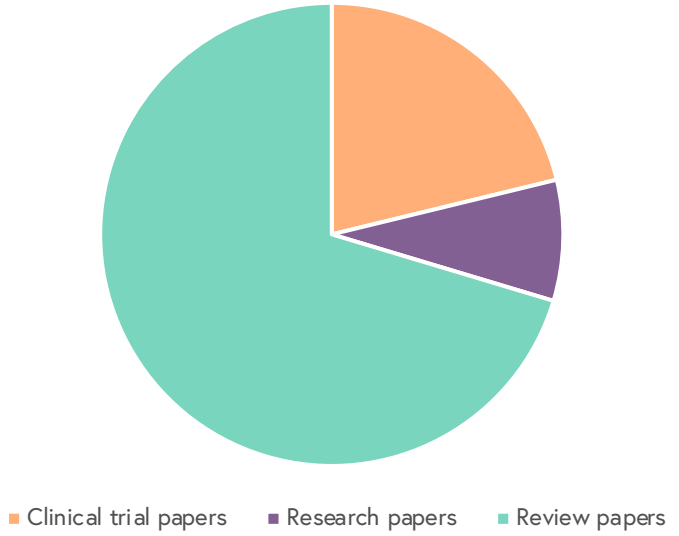
Source: Nordic Life Science Database, Medtrack, MSC analysis

The number of published ATMP related publications have decreased during the last years in Denmark

Number of ATMP related publications, from Danish affiliations (2009-2020)*



Publications 2009-2019 divided on publication type



- 415 publications related to ATMP have been published between 2009-2019.
- Among these, 88 papers have been categorized as relating to clinical trials.

* PubMed indexing for MeSH terms typically is lagging (~6-9 months). The data for 2019 should therefore not be interpreted as the complete dataset.

NOTE
The publications have at least one author connected to a Danish university, also called affiliation.

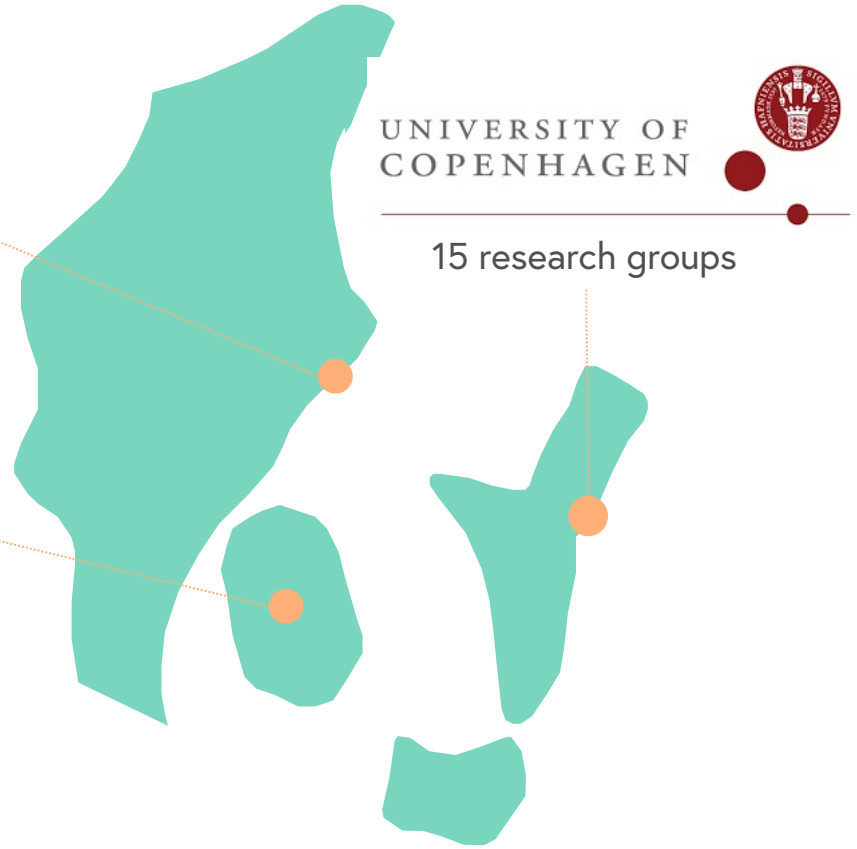
Source: PubMed (see appendix for methodology), MSC analysis

31 relevant research groups focusing on ATMP research were identified in Denmark

AARHUS UNIVERSITY
8 research groups

UNIVERSITY OF COPENHAGEN
15 research groups

SDU
University of Southern Denmark
8 research groups



Top Danish affiliations

BASED ON THE HIGHEST NUMBER OF RESEARCHERS

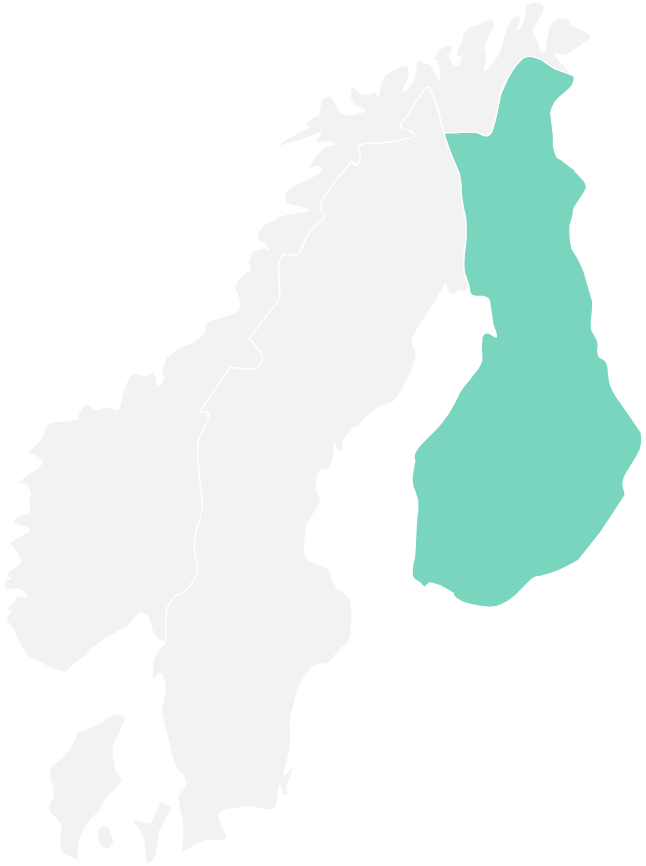
- University of Copenhagen
- University of Southern Denmark
- Aarhus University

The following criteria defined a relevant research group: Having active research within therapeutic applications in ATMP (analyzed by publications), being active at one of the top three universities when ranking by number of publications in ATMP.

Source: Monocl Professional (www.monocl.com, database accessed on Nov-Dec 2020, full methodology in Appendix), MSC analysis

FINLAND

In relation to its low publication rate, Finland holds many companies within the ATMP field



A summary of the ATMP field in Finland

- There are 6 national companies developing therapies in ATMPs.
- Within those 6 companies, there are 9 development programs ongoing where most of these programs were identified as being in early development stages.
- The majority of projects in Finland are GTMP projects.
- Published ATMP related research connectected to Finnish affiliations has remained relatively constant over the past 10 years.
- 17 research groups were identified as being focused on ATMP research.
- In addition to the above, there is 1 international company that has shown signs of ATMP development in Finland.

There are currently 6 SME companies with therapeutic ATMP R&D activity in Finland

StemSight vision unlimited — Tampere

Kuopio

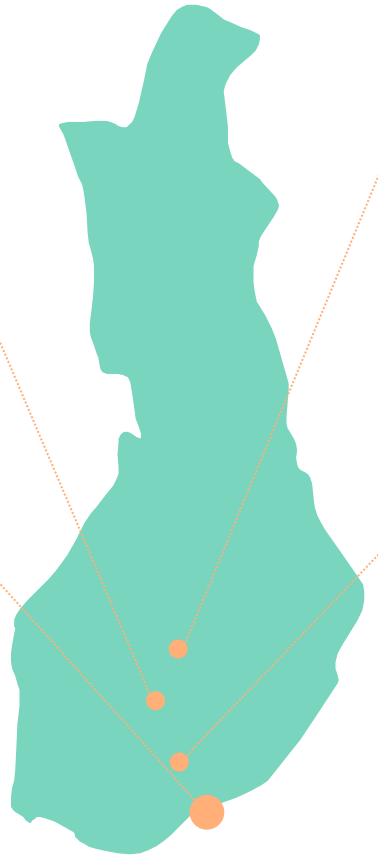
AUREALIS PHARMA

F/K/D

Helsinki

tilt BIOTHERAPEUTICS

VALO THERAPEUTICS



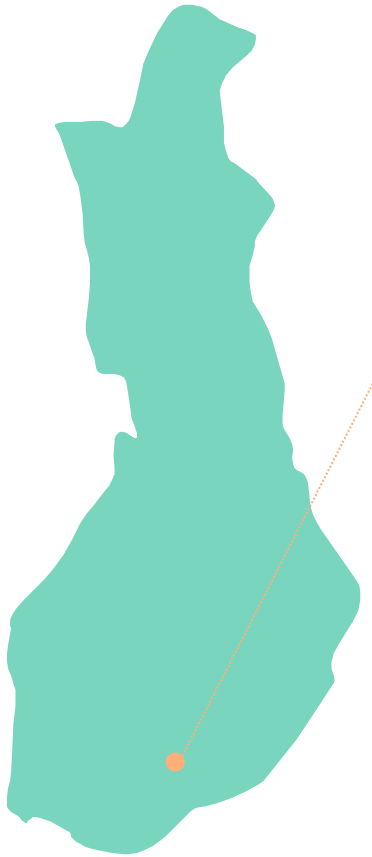
Espoo

HERANTIS PHARMA

The SME companies are defined by being founded and having their main operating activity in Finland. The maturity level varies, but all have development programs in preclinical or clinical stage.

Source: Nordic Life Science Database, Biomedtracker, MSC analysis, Interviews

1 international company was identified with ATMP-related R&D activities in Finland



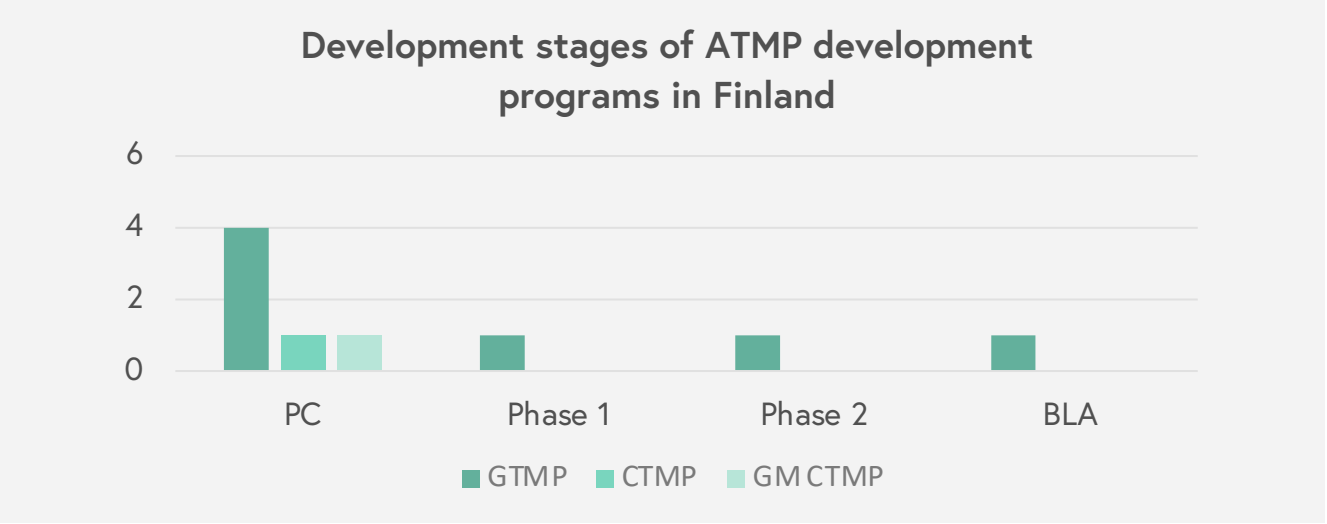
Espoo

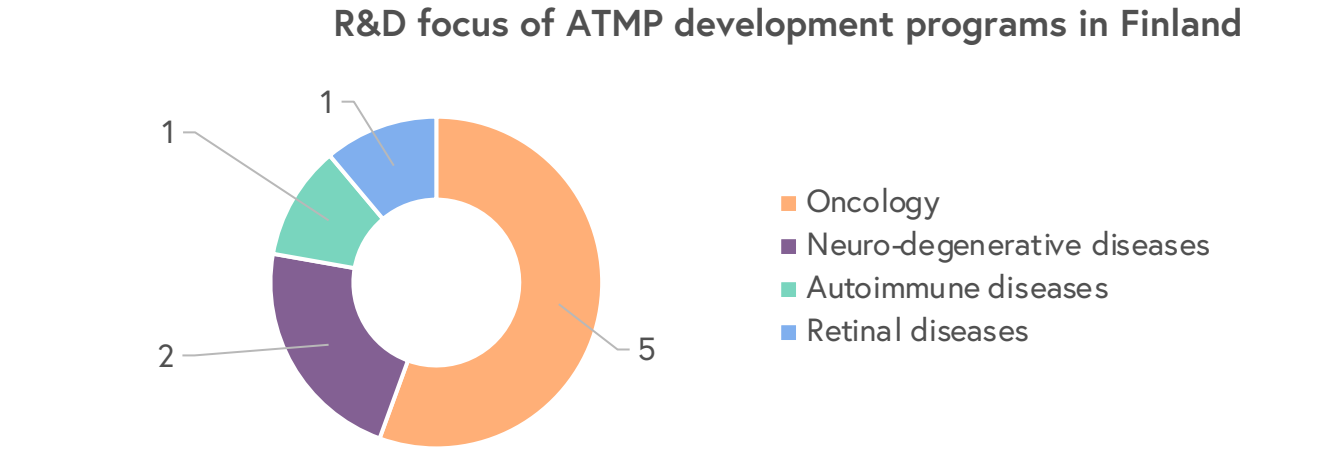
ORION PHARMA

The international companies are defined by being global players as well as having approved products, inhouse production of APIs and ATMP related R&D activities within Finland.

Source: Source: Company website, MSC analysis

A majority of the 9 ATMP development programs that are being developed by Finnish SME companies are in preclinical stage





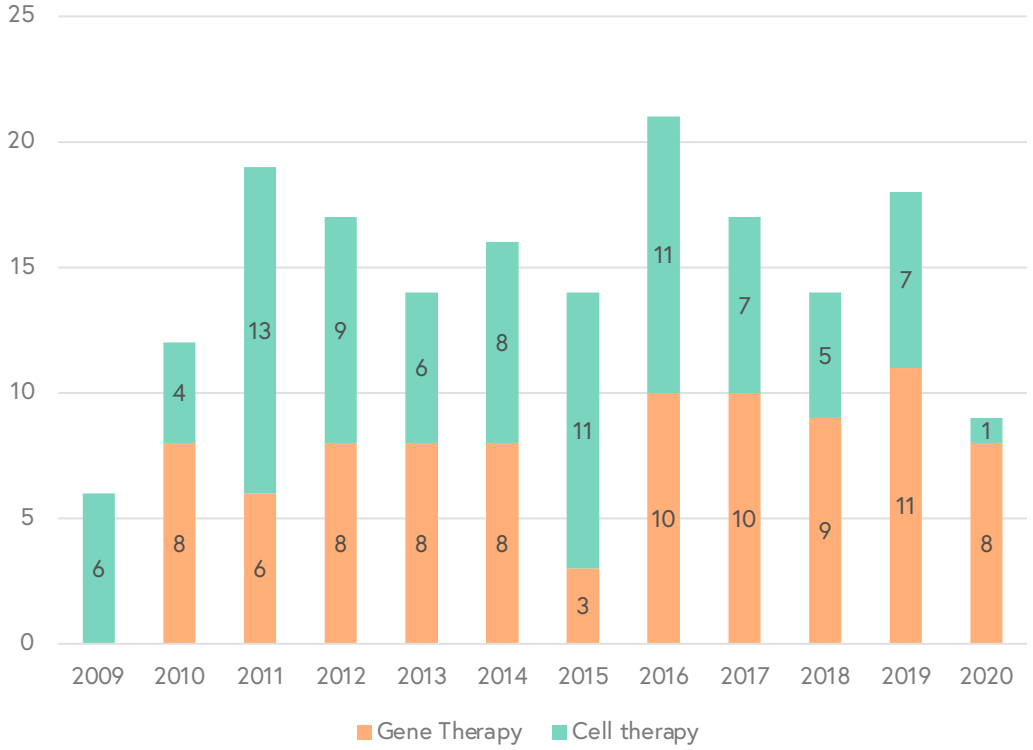
ATMP development programs in Finland

- A total of 9 ATMP development programs were identified as being in active development by the 6 SME ATMP companies in Finland.
- Most of these programs were identified as still being in early development stages.
- A majority of these programs are focused on oncology and neuro-degenerative diseases.
- One active program, a GTMP, is developing a Phase 2 therapy, which is in breast cancer associated secondary lymphedema (Herantis).
- One of these programs, a GTMP project by FKD Therapies, is in the process of biologics license application (BLA) and could soon be approved for bladder cancer.

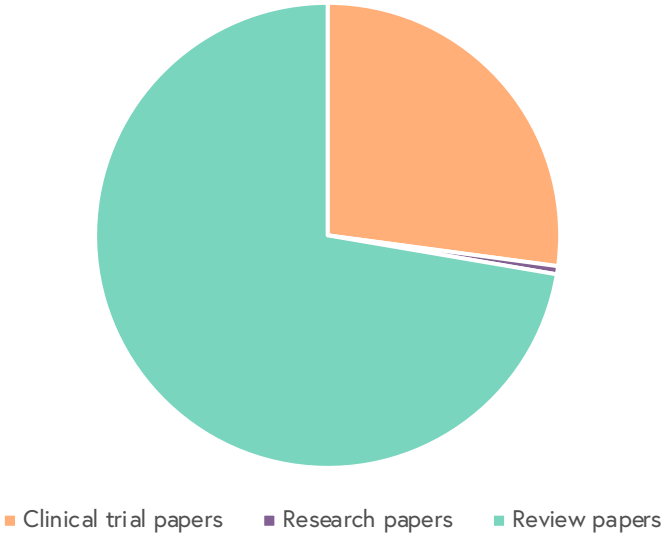
Source: Nordic Life Science Database, Medtrack, MSC analysis

Published ATMP related research has remained relatively constant over the past 10 years, ranging between 6 and 21 publications

Number of ATMP related publications, from Finnish affiliations (2009-2020)*



Publications 2009-2019 divided on publication type



- 177 publications related to ATMP has been published between 2009-2019.
- Among these, 48 papers have been categorized as relating to clinical trials.

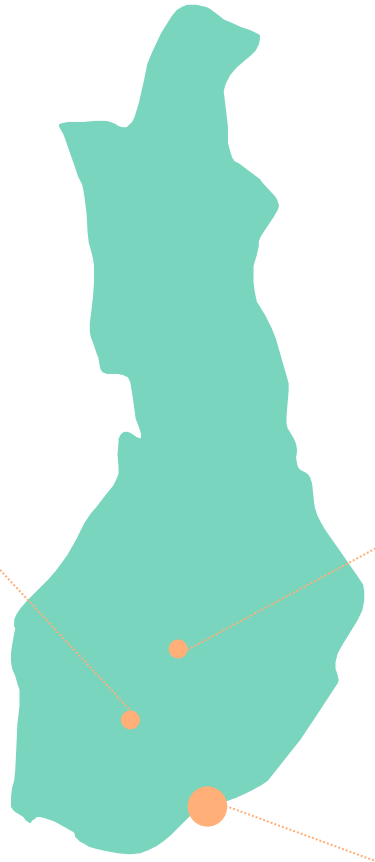
* PubMed indexing for MeSH terms typically is lagging (~6-9 months). The data for 2019 should therefore not be interpreted as the complete dataset.

NOTE
The publications have at least one author connected to a Finnish university, also called affiliation.

Source: PubMed (see appendix for methodology), MSC analysis

17 relevant research groups focusing on ATMP research were identified in Finland

Tampere University
2 research groups



UNIVERSITY OF EASTERN FINLAND
5 research groups

UNIVERSITY OF HELSINKI
9 research groups

Other renowned universities with research groups

UNIVERSITY OF OULU
1 research group

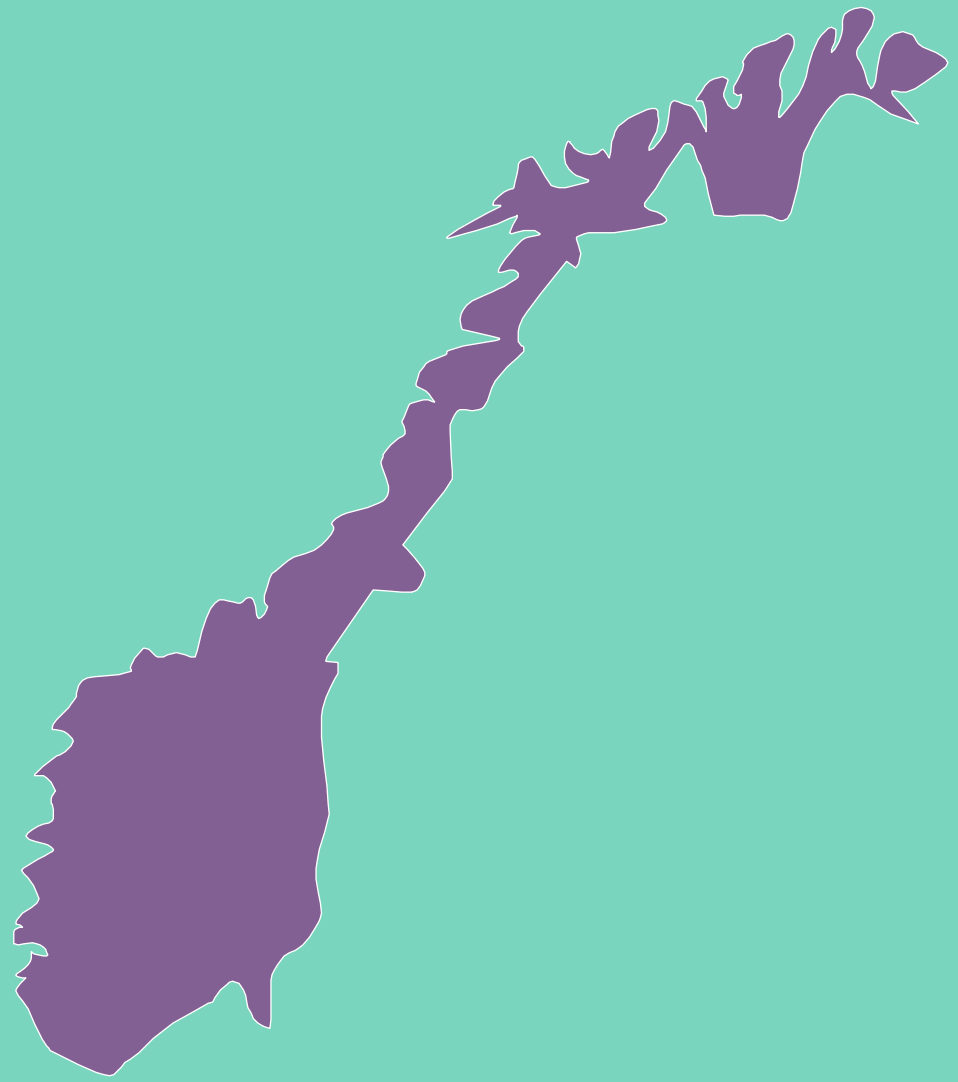
Top Finnish affiliations

BASED ON THE HIGHEST NUMBER OF RESEARCHERS

- University of Helsinki
- University of Eastern Finland
- Tempere University

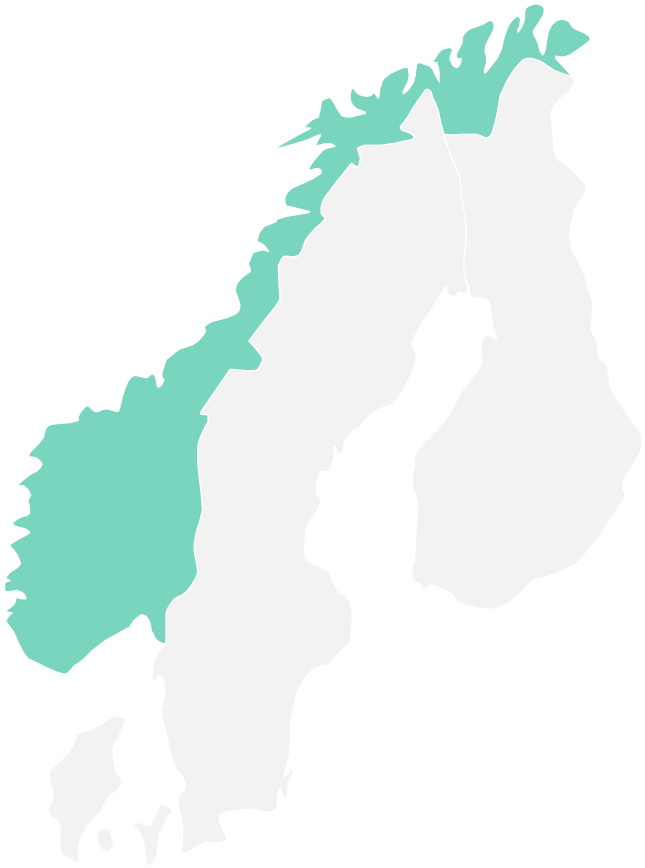
The following criteria defined a relevant research group: Having active research within therapeutic applications in ATMP (analyzed by publications), being active at one of the top three universities when ranking by number of publications in ATMP.

Source: Monocl Professional (www.monocl.com, database accessed on Nov-Dec 2020, full methodology in Appendix), MSC analysis



NORWAY

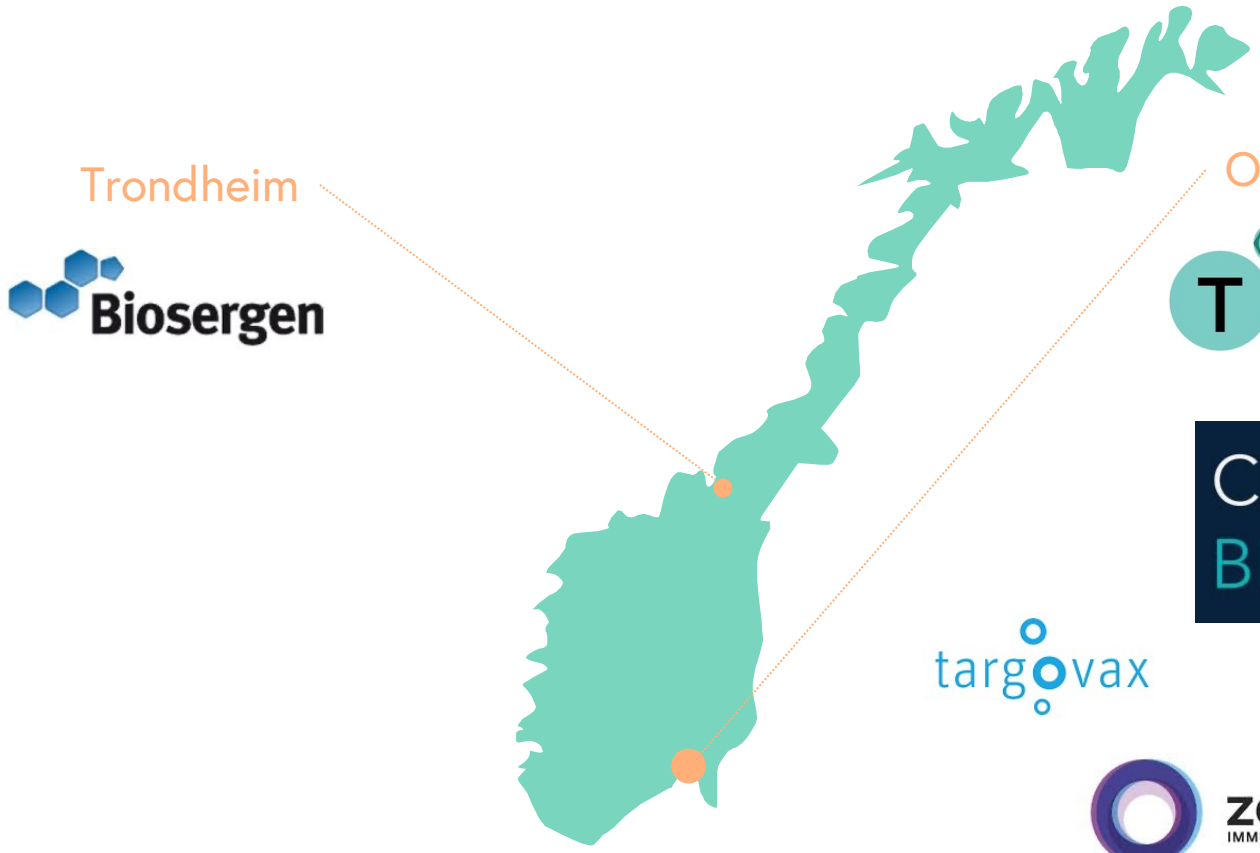
In relation to its low publication rate, Norway holds many companies within the ATMP field



A summary of the ATMP field in Norway

- There are 5 national companies developing therapies in ATMPs.
- Within those 5 companies, there are 12 development programs ongoing where most of these programs were identified as being in early development stages.
- There is an equal amount of GTMP and GM CTMP projects in Norway. These make out the largest part of the total amount of projects.
- Most development programs are related to oncology.
- The number of publications related to ATMP research show a slightly declining trend over the past 10 years, and range between 8 and 21 publications annually.
- 12 research groups were identified as being focused on ATMP research.
- There are no International companies that have shown signs of ATMP development in Norway.

There are currently 5 SME companies with therapeutic ATMP R&D activity in Norway



Biosergen

T HELPER Cellular Therapies

CLEX BIO

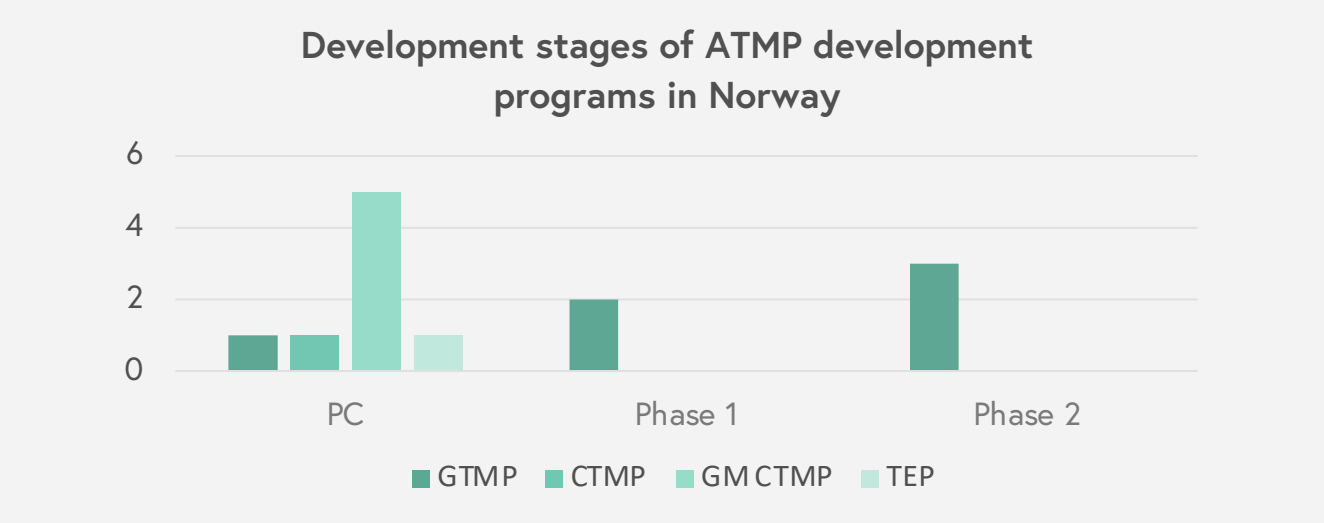
targovax

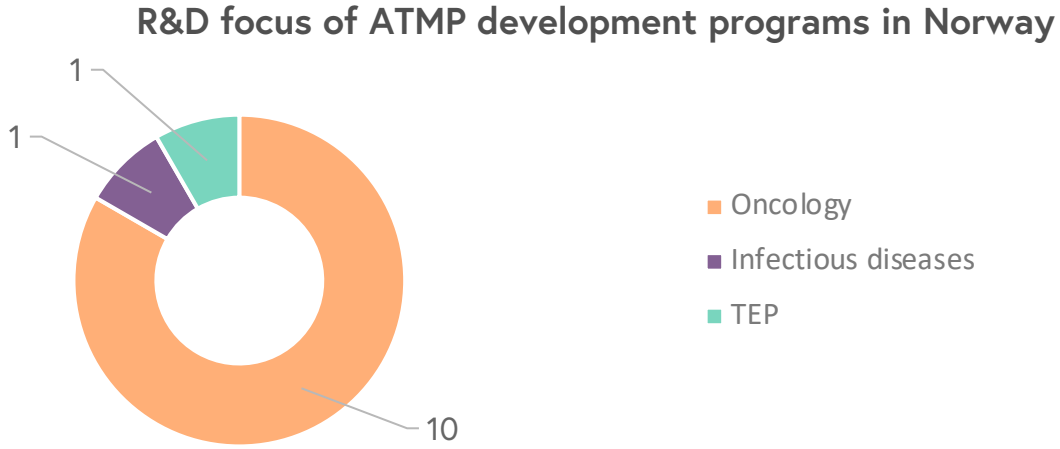
zelluna IMMUNOTHERAPY

The SME companies are defined by being founded and having their main operating activity in Norway. The maturity level varies, but all have development programs in preclinical or clinical stage.

Source: Nordic Life Science Database, Biomedtracker, MSC analysis, Interviews

A majority of the 12 ATMP development programs are being developed by national Norwegian companies are in preclinical stage





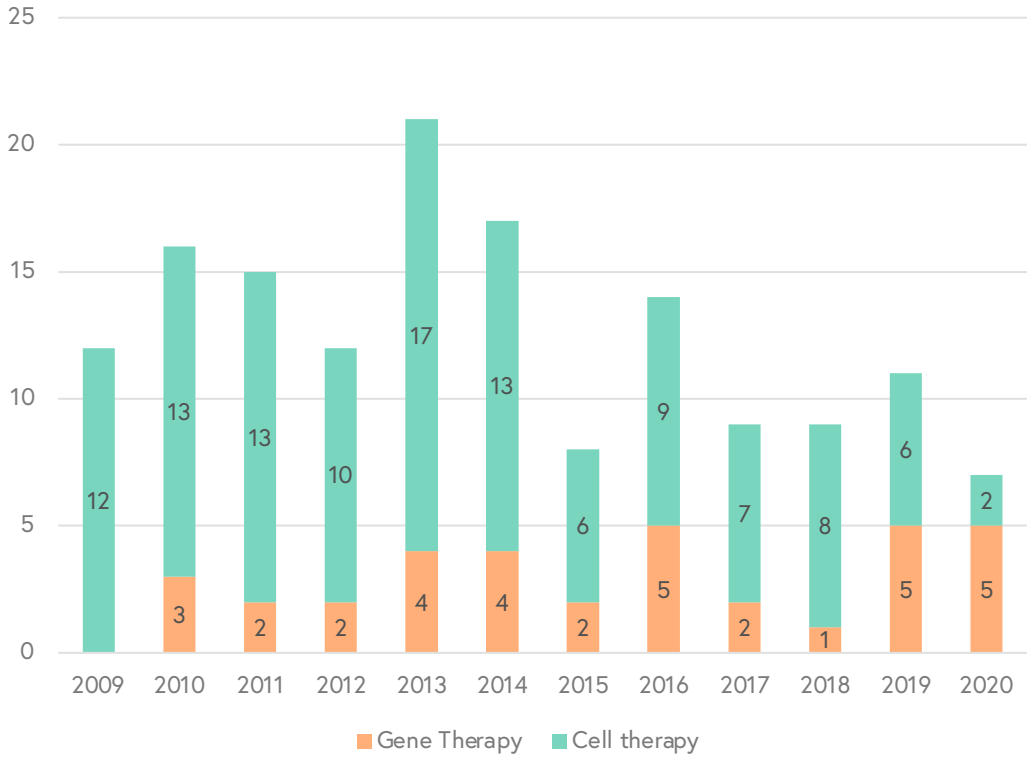
ATMP development programs in Norway

- A total of 12 ATMP programs were identified as being in active developmentby the 5 SME ATMP companies in Norway.
- Most of these programs were identified as being in early development stages.
- Almost all these programs are focused on oncology.
- Targovax is the only company in clinical phase.

Source: Nordic Life Science Database, Medtrack, MSC analysis

The number of publications related to ATMP research show a slightly declining trend over the past 10 years

Number of ATMP related publications, from Norwegian affiliations (2009-2020)*



Publications 2009-2019 divided on publication type

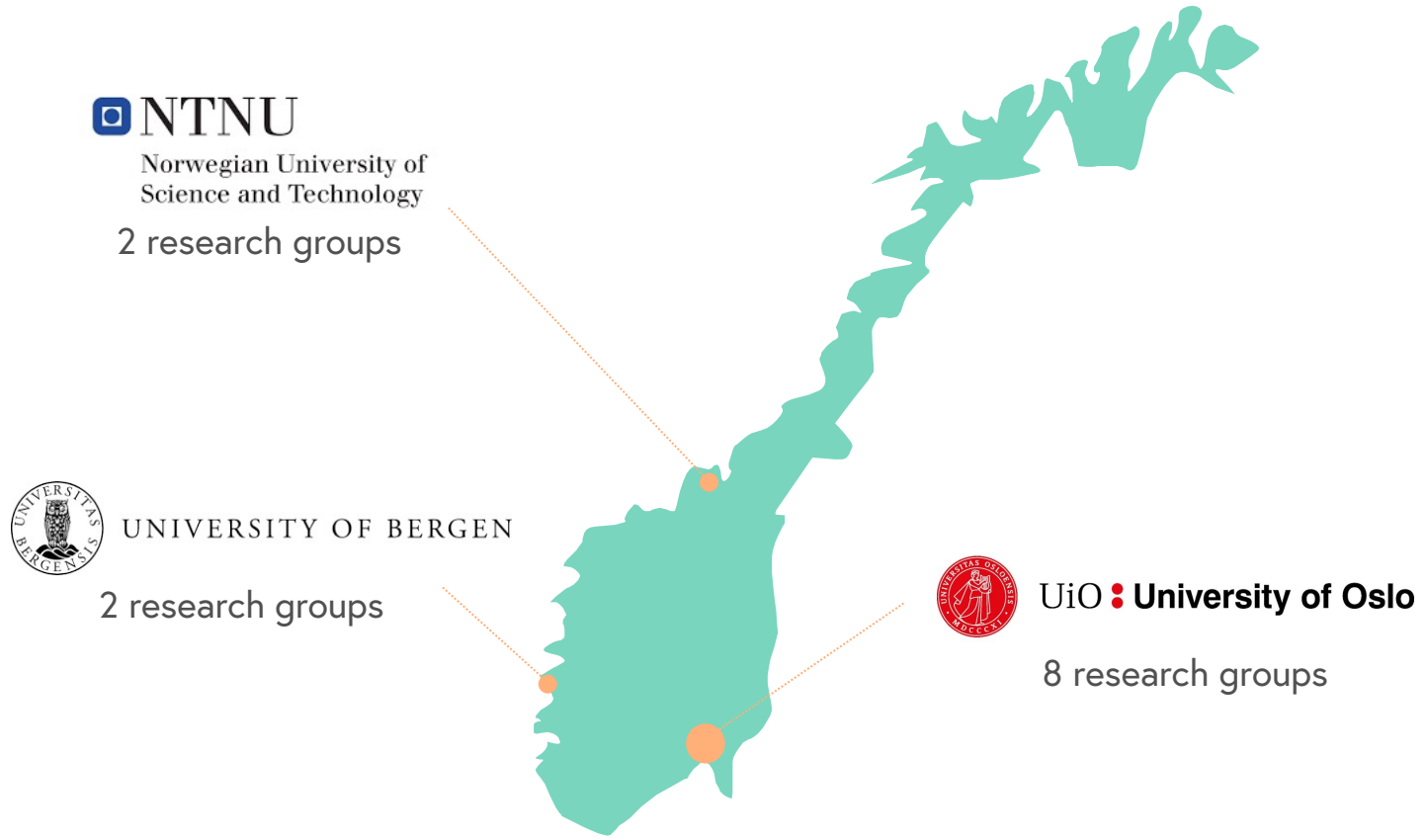
- 151 publications related to ATMP has been published between 2009-2019.
- Among these, 62 papers have been categorized as relating to clinical trials.

* PubMed indexing for MeSH terms typically is lagging (~6-9 months). The data for 2019 should therefore not be interpreted as the complete dataset.

NOTE
The publications have at least one author connected to a Norwegian university, also called affiliation.

Source: PubMed (see appendix for methodology), MSC analysis

12 relevant research groups focusing on ATMP research were identified in Norway



Top Norwegian affiliation

BASED ON THE HIGHEST NUMBER OF RESEARCHERS

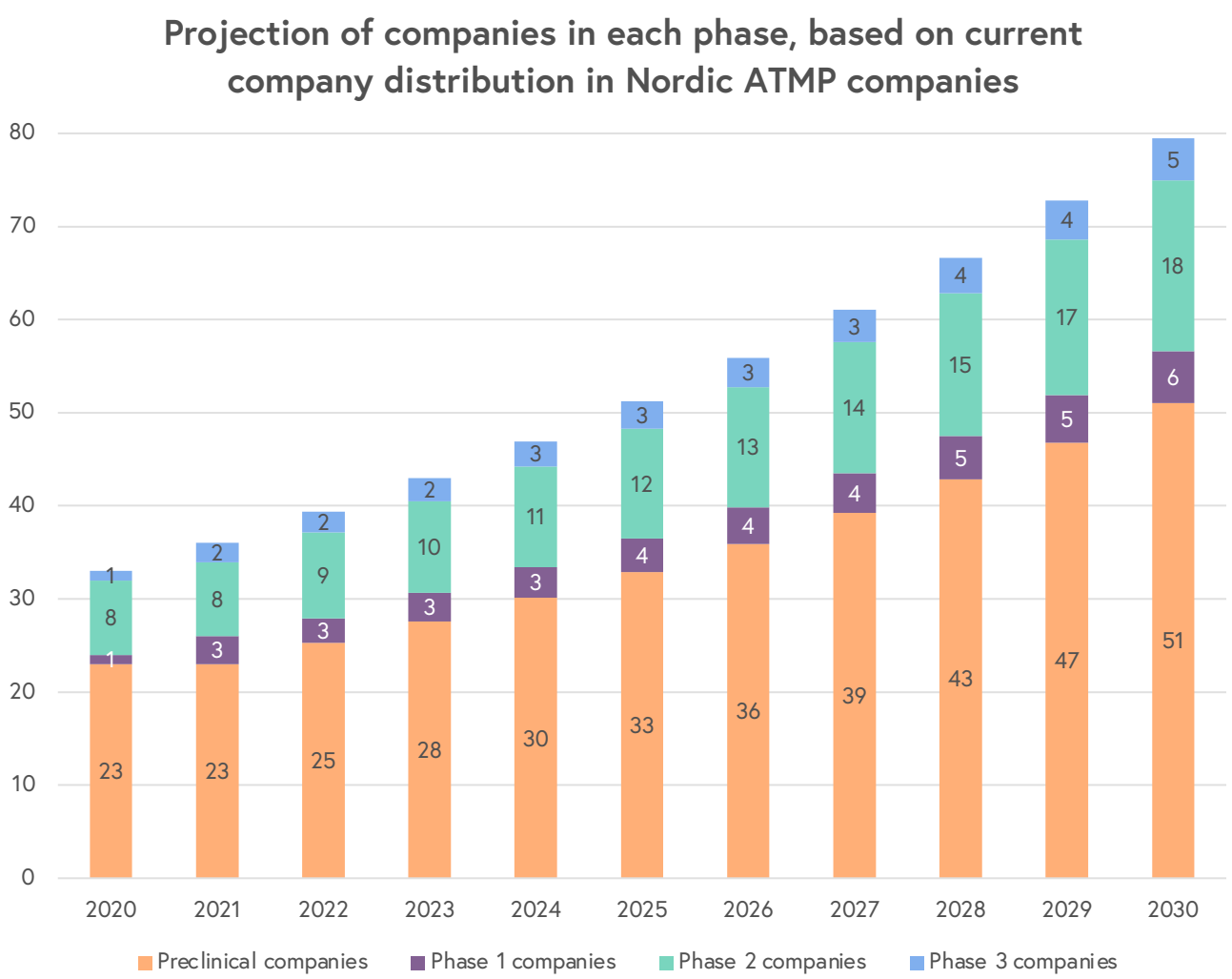
- University of Oslo
- University of Bergen
- Norwegian University of Science and Technology

The following criteria defined a relevant research group: Having active research within therapeutic applications in ATMP (analyzed by publications), being active at one of the top three universities when ranking by number of publications in ATMP.

Source: Monocl Professional (www.monocl.com, database accessed on Nov-Dec 2020, full methodology in Appendix), MSC analysis

Projected scale of a Nordic ATMP infrastructure organization

The number of ATMP companies in the Nordics, are expected to increase to about 80 companies by 2030 from 33 in 2020



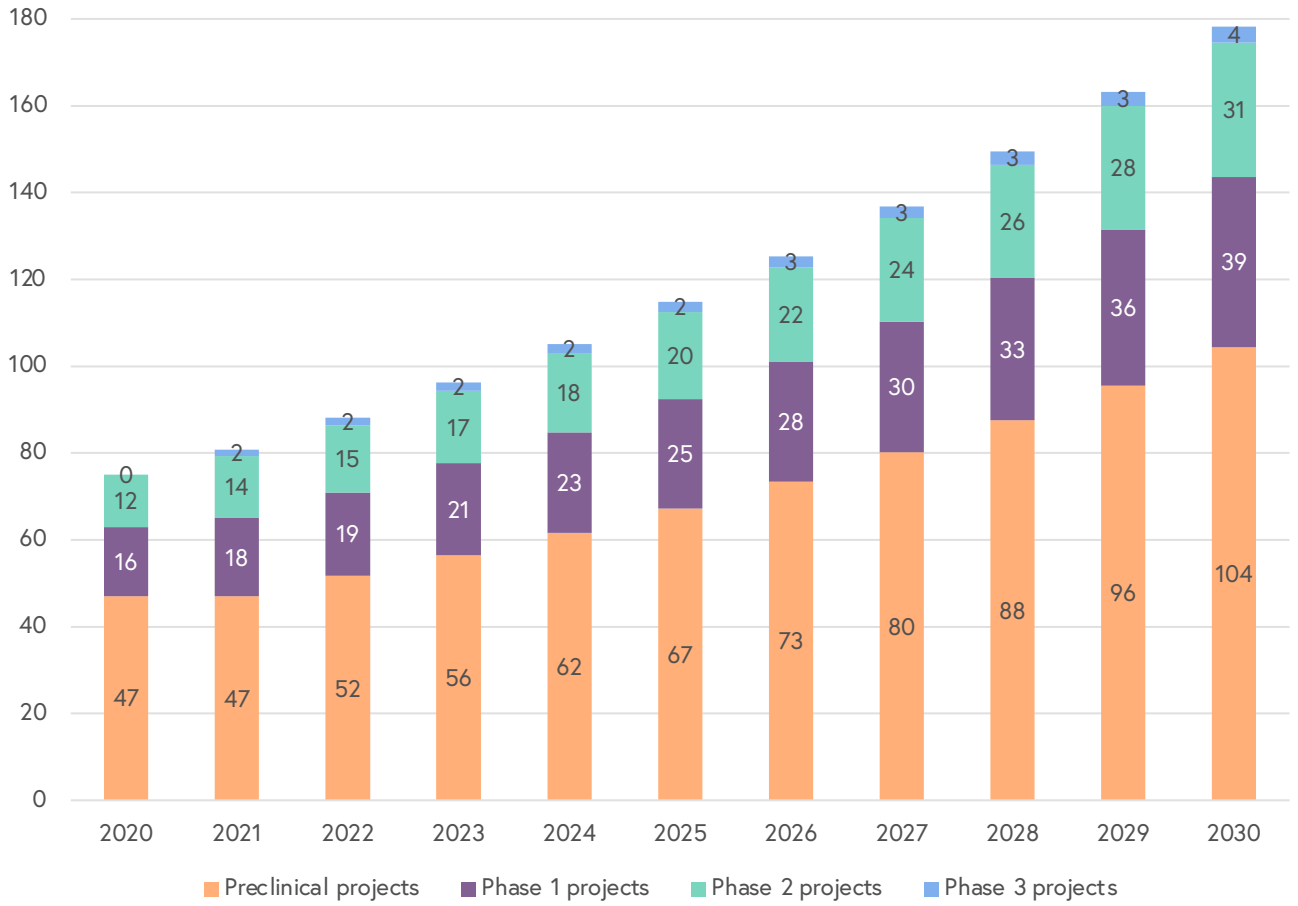
Key assumptions

- 2020 number of companies and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- The growth rate of 109% from 2020 to 2030 was compiled by four sets of growth calculations;
  - A Compound Annual Growth Rate (CAGR) based on the number of ATMP trials in Europe was added to account for growth in the market.
  - A CAGR based on a similar organization's growth data.
  - A CAGR based on the growth in Nordic companies 2018-2020.
  - A CAGR based on the historical average number of companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

The total number of ATMP projects in the Nordics are expected to increase from 75 to 174 between 2020 and 2030

Projection of companies in each phase, based on current project distribution in Nordic ATMP projects



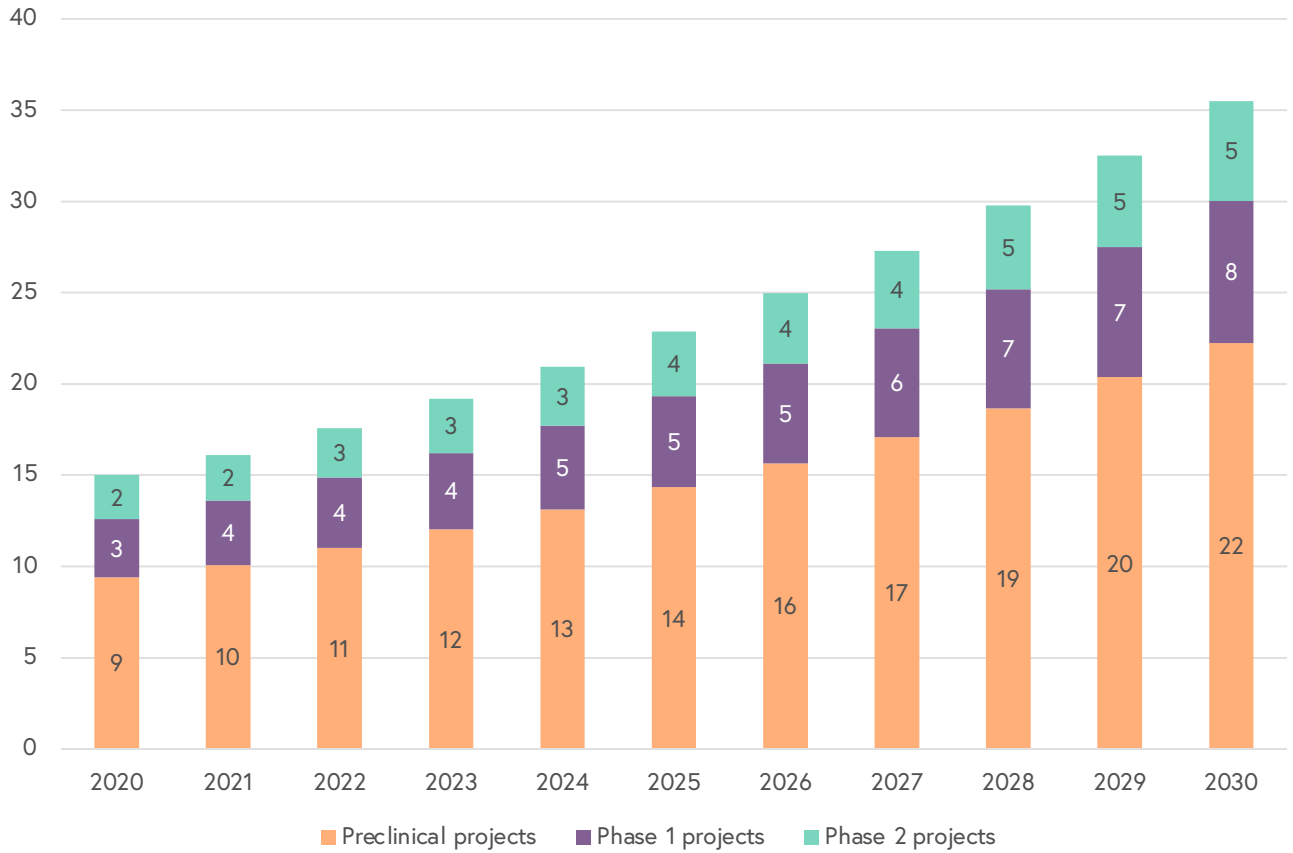
Key assumptions

- 2020 number of projects and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- The growth rate of 109% from 2020 to 2030 was compiled by four sets of growth calculations;
  - A CAGR based on the number of ATMP trials in Europe was added to account for growth in the market.
  - A CAGR based on a similar organization's growth data.
  - A CAGR based on the growth in Nordic companies 2018-2020.
  - A CAGR based on the historical average number of companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

An ATMP infrastructure organization is expected to have 35 incoming customer projects in 2030, based on a 20% market share

Projection of companies in each phase, based on current project distribution in Nordic ATMP projects and a 20% market share



Key assumptions

- **A market share of 20% was adopted.**
- **No Phase 3 projects are expected to be carried out by the organization and these were thus excluded.**
- 2020 number of projects and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- The growth rate of 109% from 2020 to 2030 was compiled by four sets of growth calculations;
  - A CAGR based on the number of ATMP trials in Europe was added to account for growth in the market.
  - A CAGR based on a similar organization's growth data.
  - A CAGR based on the growth in Nordic companies 2018-2020.
  - A CAGR based on the historical average number of companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected customer projects vary between 18 and 88 in 2030, depending on market share

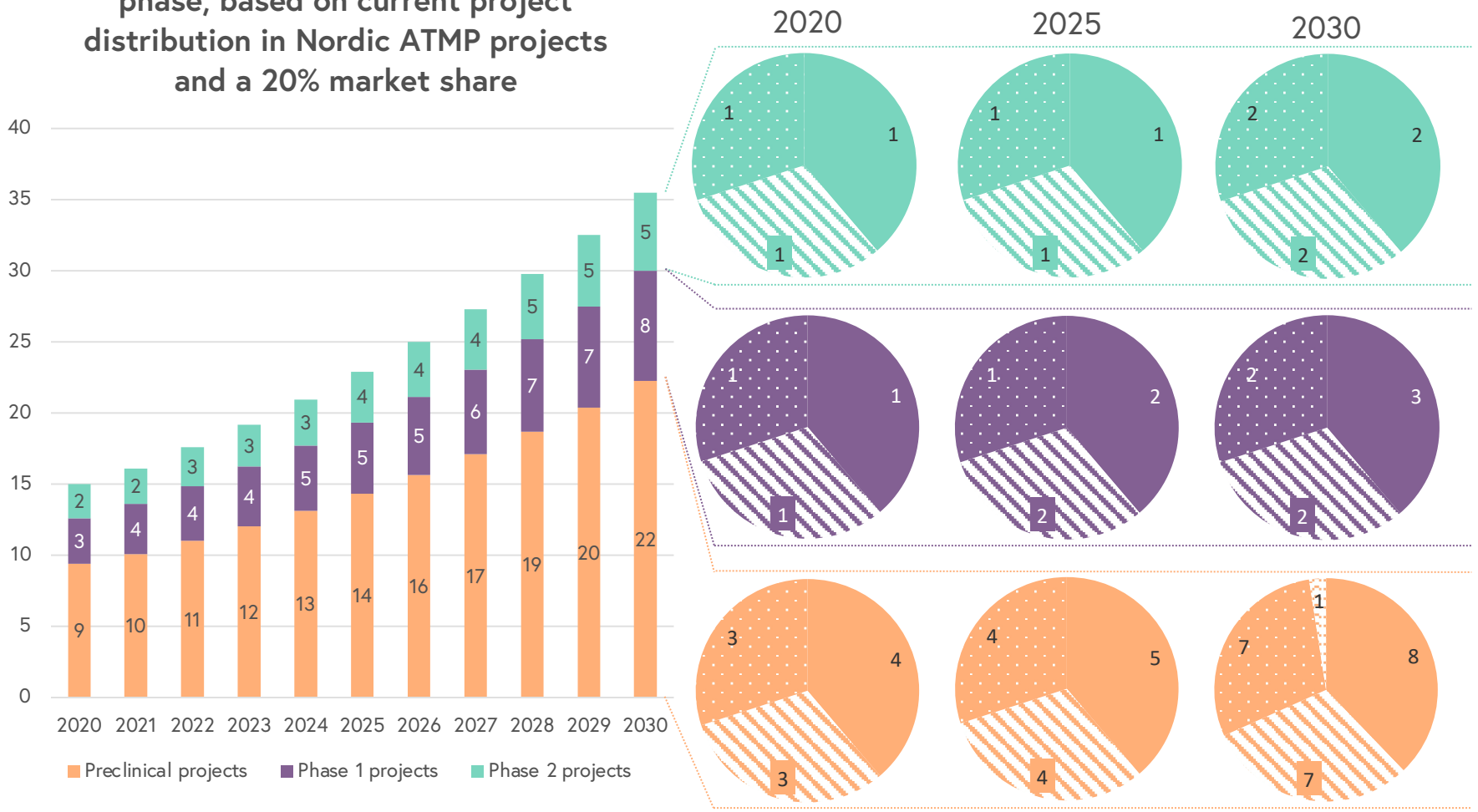
- The following sensitivity analysis was conducted due to the difficulty in foreseeing the market share that a new ATMP infrastructure organization can capture.
- The market share is expected to be 20% (base case) due to the large need in the current market, based on primary data from key players in the Nordic ATMP market.

	Market share (10%)	Market share (20%)	Market share (30%)	Market share (40%)	Market share (50%)
		Base scenario			
Number of customer projects in 2020	8	**14**	23	30	38
Number of customer projects in 2025	11	**23**	34	45	57
Number of customer projects in 2030	18	**35**	53	71	88

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

The technology division of expected customer projects is assumed to reflect 2020 numbers, but the number of projects will increase

Projection of companies in each phase, based on current project distribution in Nordic ATMP projects and a 20% market share



GM CTMP

CTMP

GTMP

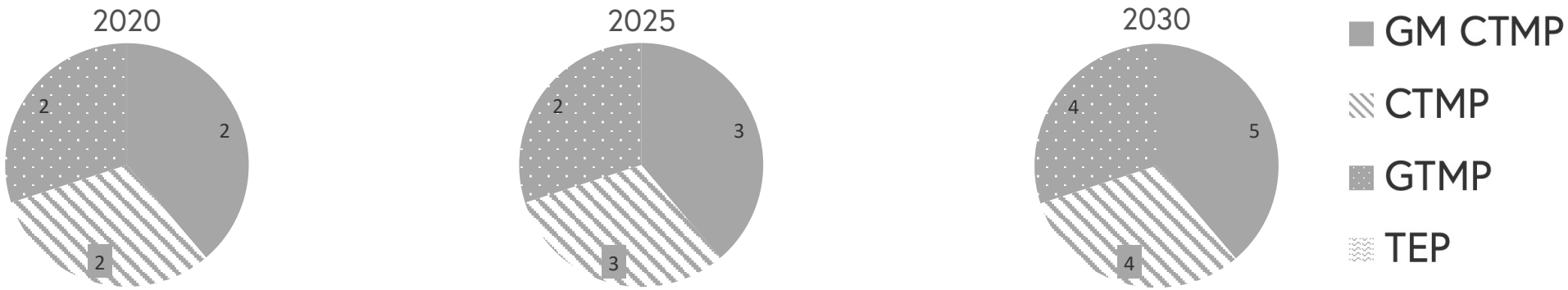
TEP

The division of company types (i.e. GM CTMP, CTMP, GTMP and TEP) was extracted from the company division in 2020. The growth could be different in the different company types, however there is no evident way to calculate for this difference.

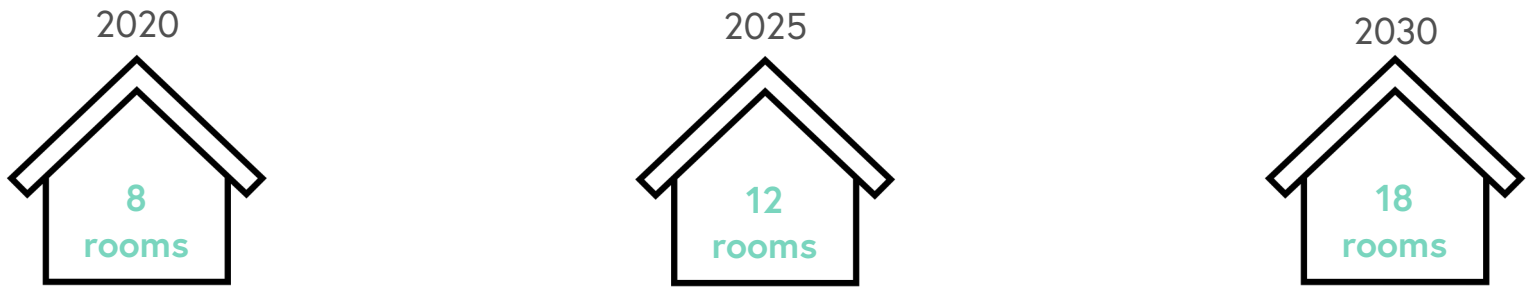
Source: MSC analysis

The need of clean rooms in an ATMP infrastructure organization is expected to increase from 8 rooms in 2020 to 18 in 2030

Phase 1 & 2 customer projects



Number of clean rooms needed for customer projects



NOTE
None of the preclinical projects are assumed to need clean rooms.
A project is assumed to occupy a clean room for one year on average, based on interviews which gave project times as follows: DNA plasmid development ~6 months, Lentiviral GMP production 9-12 months; AAV GMP production 6 months to 3 years. The GM CTMP companies are expected to need two rooms per year due to the need of both a positive and negative pressure room.

Source: MSC analysis

Appendix

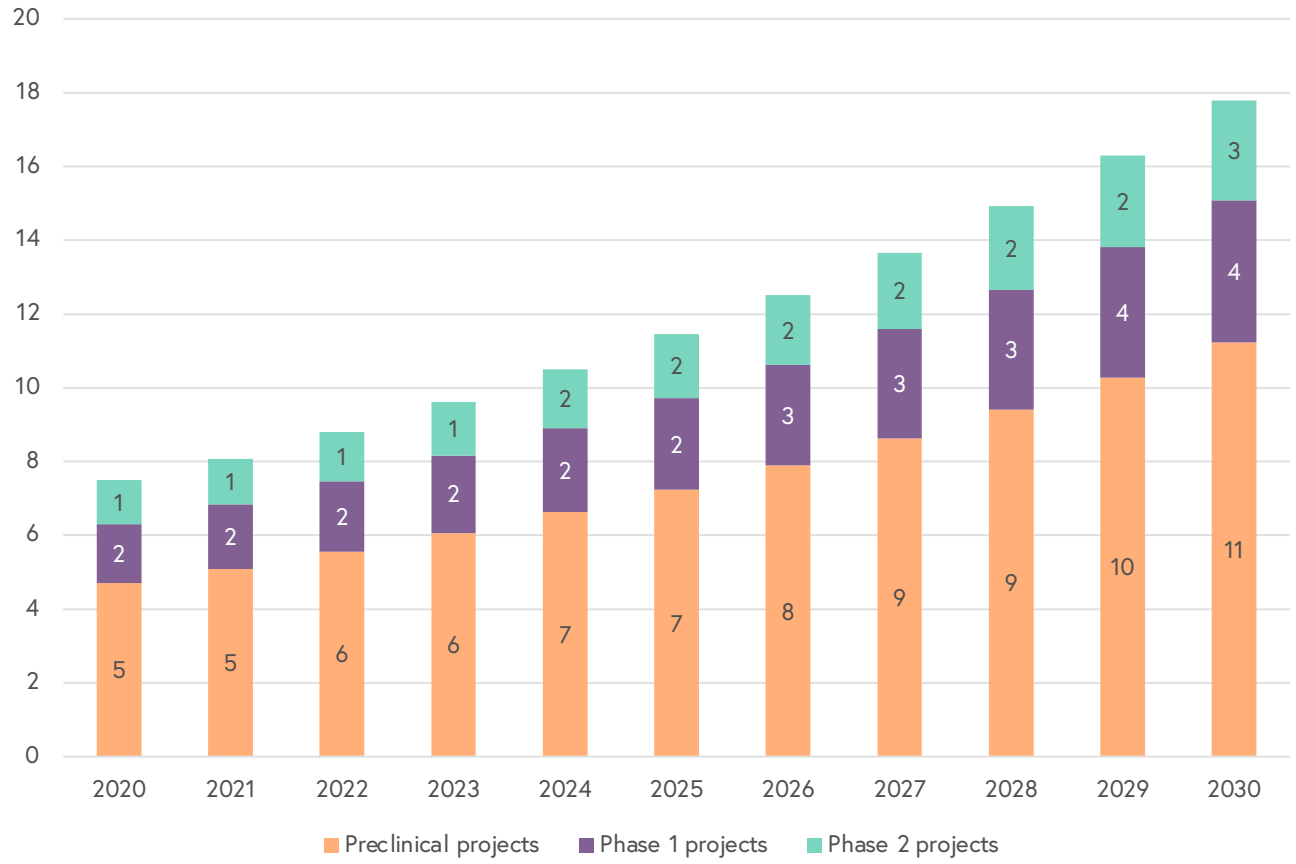
MSC | STRATEGY & COMMUNICATION

Case scenarios

MSC STRATEGY & COMMUNICATION

Number of expected customer projects in the Nordics, based on a market share of 10%

Projection of projects in each phase, based on current project distribution in Nordic ATMP companies and 30% market share



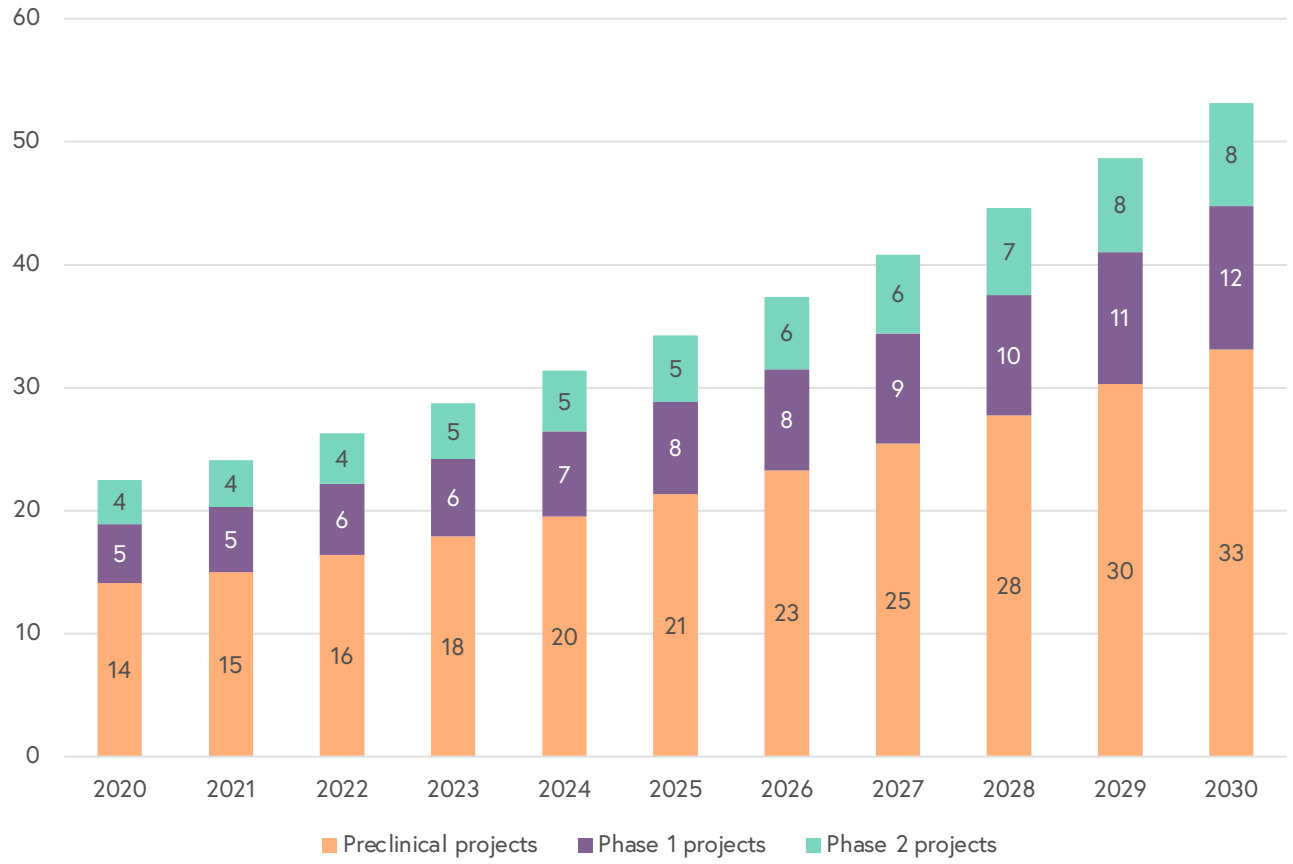
Key assumptions

- **A market share of 10% was adopted**.
- 2020 number of projects and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- The growth rate of 109% from 2020 to 2030 was compiled by four sets of growth calculations;
  - A CAGR based on the number of ATMP trials in Europe was added to account for growth in the market.
  - A CAGR based on a similar organization's growth data.
  - A CAGR based on the growth in Nordic companies 2018-2020.
  - A CAGR based on the historical average number of companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected customer projects in the Nordics, based on a market share of 30%

Projection of projects in each phase, based on current project distribution in Nordic ATMP companies and 30% market share

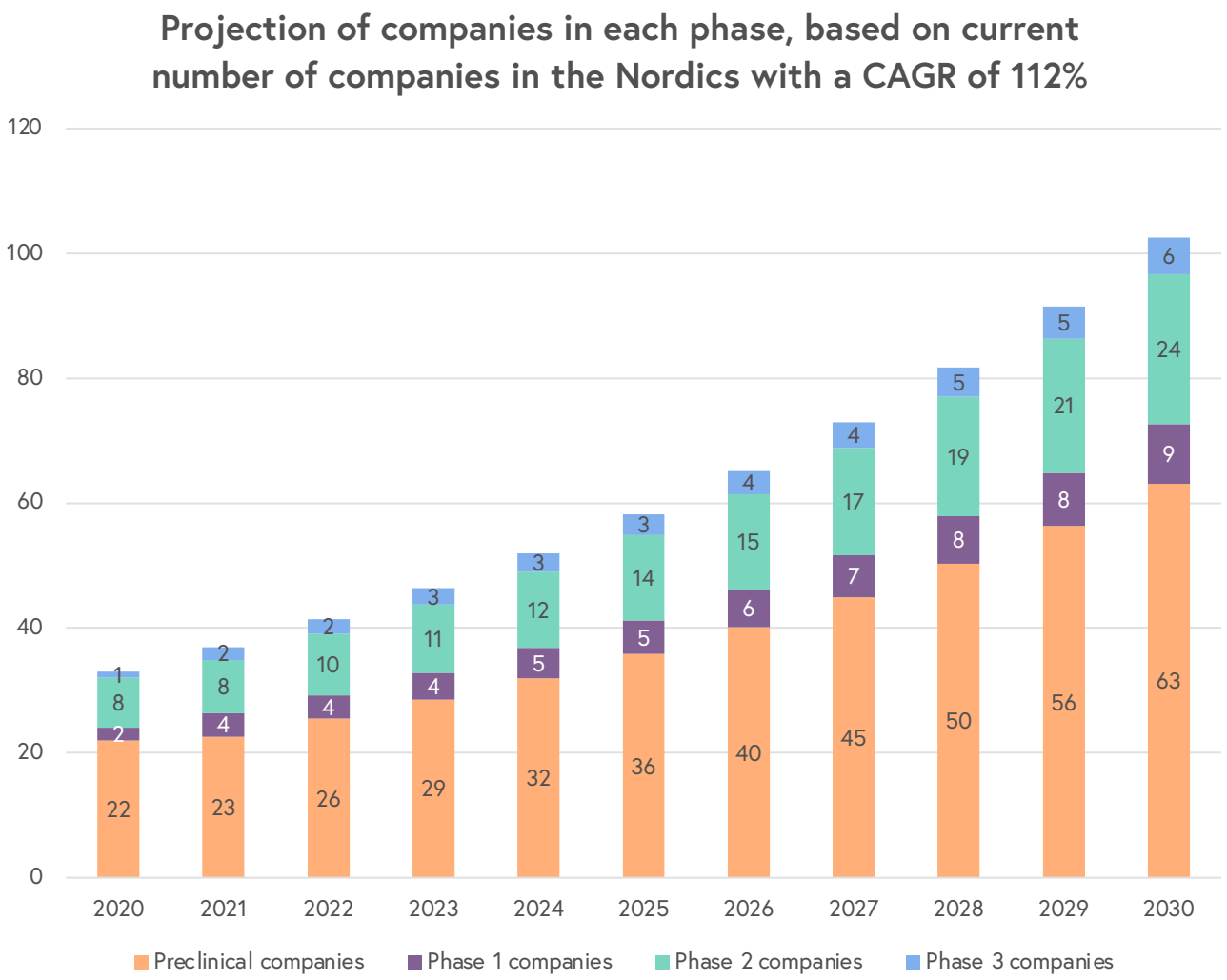


Key assumptions

- **A market share of 30% was adopted**.
- 2020 number of projects and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- The growth rate of 109% from 2020 to 2030 was compiled by four sets of growth calculations;
  - A CAGR based on the number of ATMP trials in Europe was added to account for growth in the market.
  - A CAGR based on a similar organization's growth data.
  - A CAGR based on the growth in Nordic companies 2018-2020.
  - A CAGR based on the historical average number of companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected ATMP companies in the Nordics, based on growth according to ATMP trials



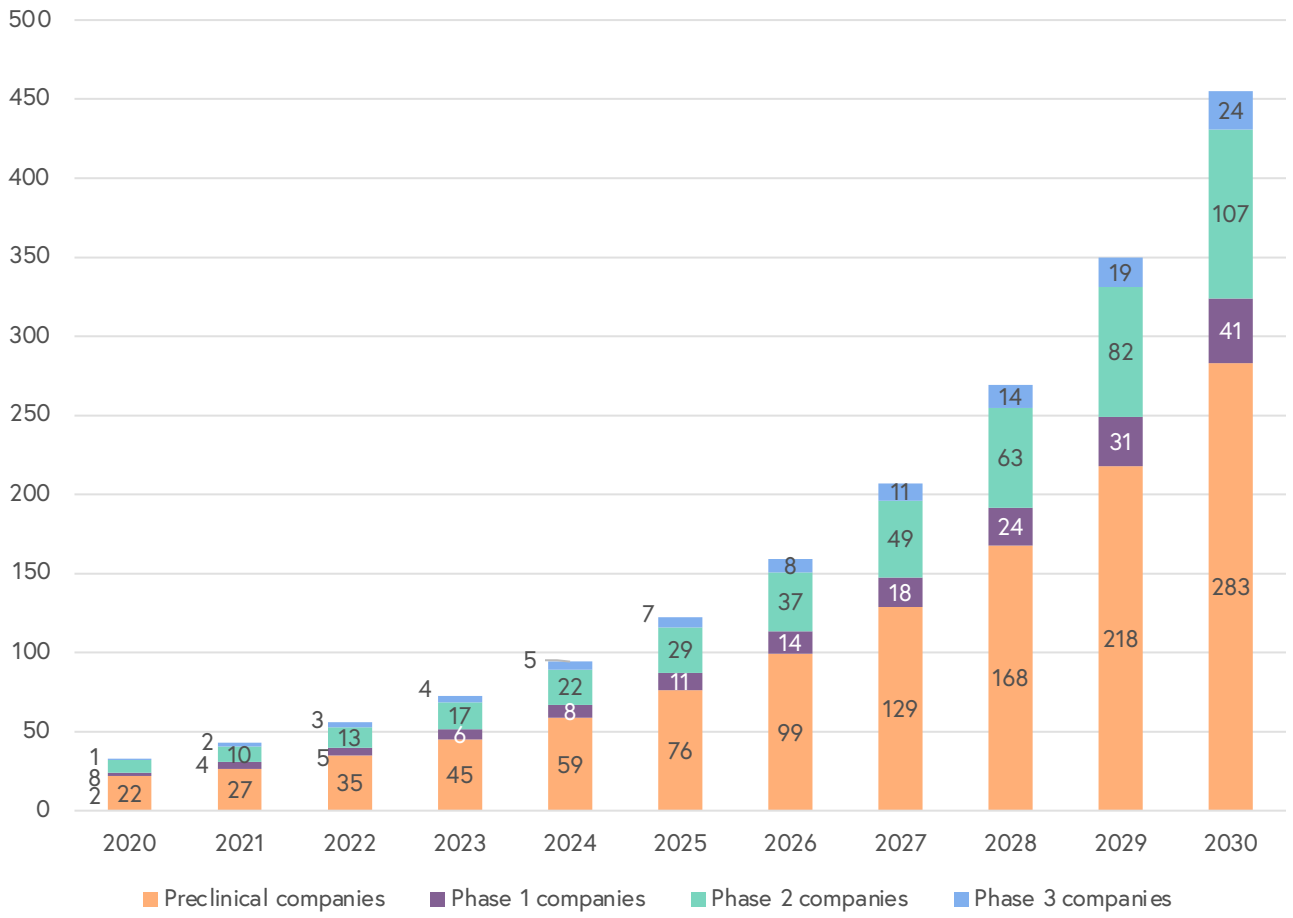
Key assumptions

- 2020 number of companies and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- **The growth was based on a CAGR of 112%, based on the growth ATMP related trials in Europe 2018-2020.**

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected ATMP companies in the Nordics, based on a similar organization's growth data

Projection of companies in each phase, based on current number of companies in the Nordics with a CAGR of 130%

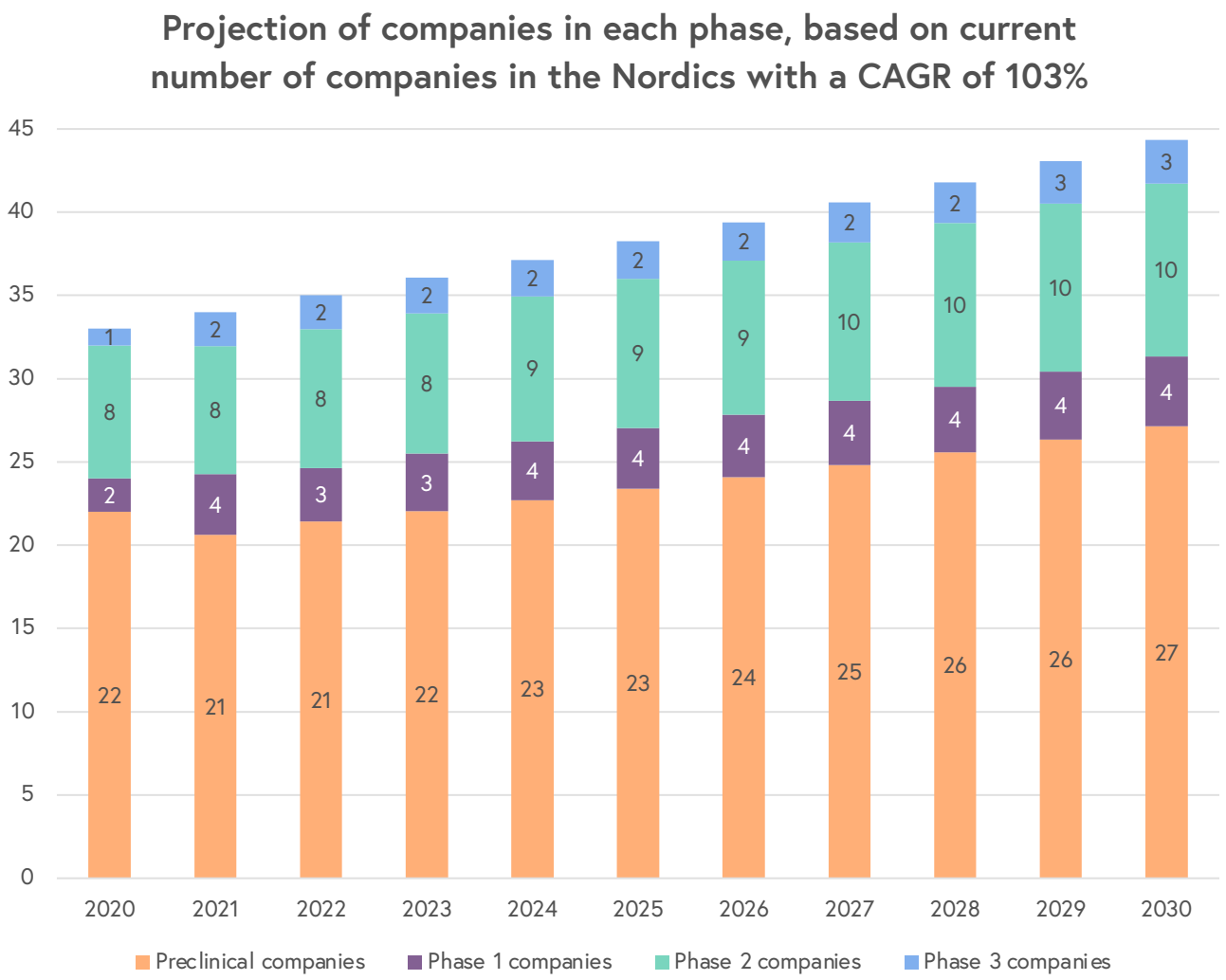


Key assumptions

- 2020 number of companies and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- **The growth was based on a CAGR of 130%, based on a similar organization's growth data.**

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected ATMP companies in the Nordics, based on growth in Nordic ATMP companies in near time



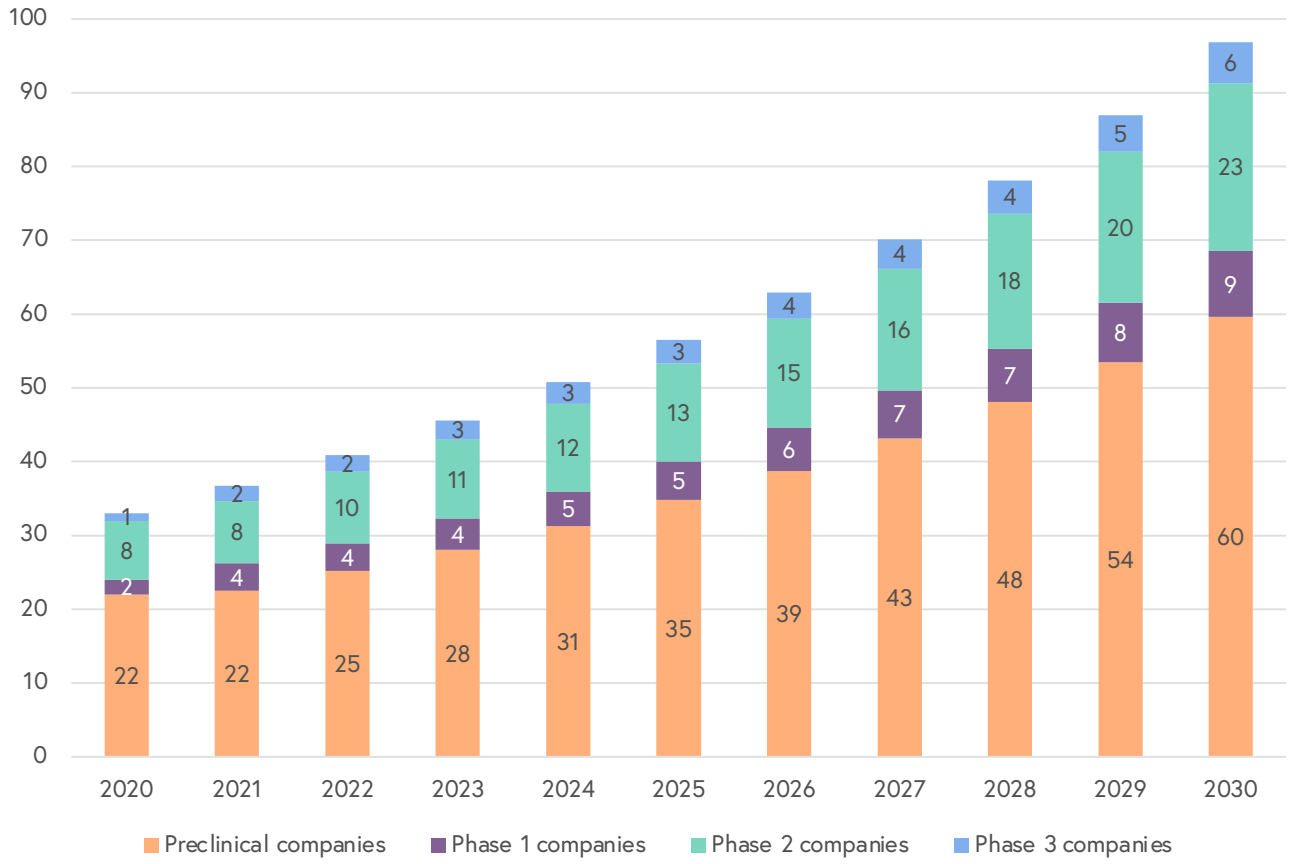
Key assumptions

- 2020 number of companies and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- **The growth was based on a CAGR of 103%, based on the growth in Nordic ATMP companies 2018-2020.**

Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Number of expected ATMP companies in the Nordics, based on growth in Nordic ATMP companies long-term

Projection of companies in each phase, based on current number of companies in the Nordics with a growth factor of 111%



Key assumptions

- 2020 number of companies and distribution between phases was used.
- Assumed amount of time in trials was 13 years, based on marketed products:
  - Preclinical: 4 years
  - Phase 1: 3 years
  - Phase 2: 3 years
  - Phase 3: 3 years
- The phase success was based on Hay et al. (2014) for biologics and Takebe et al. (2018).
- **The growth was based on a growth factor of 111%, based on the historical average number of ATMP companies founded in the Nordics 2015-2020, based on companies identified in earlier parts of this report.**

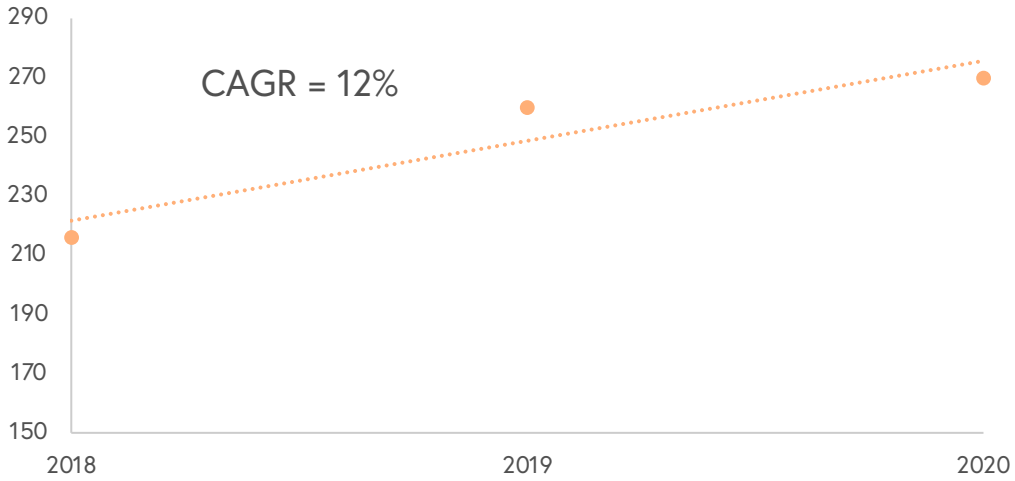
Source: MSC analysis; ARM Annual reports; Hay, M., et al., 2014. Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), pp.40-51.; Takebe, T., et al., 2018, The Current Status of Drug Discovery and Development as Originated in United States Academia: The Influence of Industrial and Academic Collaboration on Drug Discovery and Development

Additional market and growth data

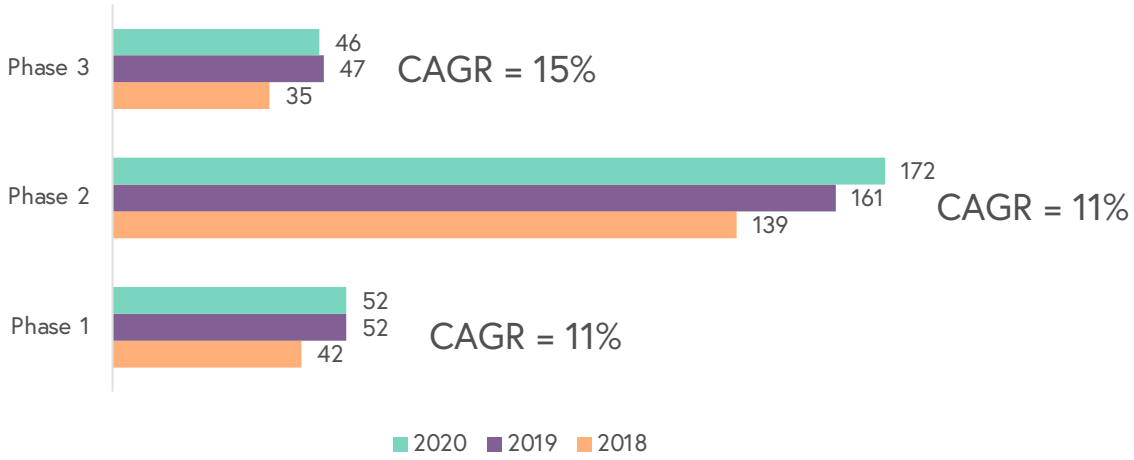
Measuring the growth of the ATMP market in terms of growth of clinical trials in ATMP yields a CAGR of 11-15%

The number of clinical trials within ATMPs are growing in Europe and Israel. Phase 3 trials have seen the largest in growth during the last few years, even though the number of trials decreased by one in 2020.

# of ATMP related trials sponsored by European or Israeli therapeutic developer, all phases



# of ATMP related trials sponsored by European or Israeli therapeutic developer

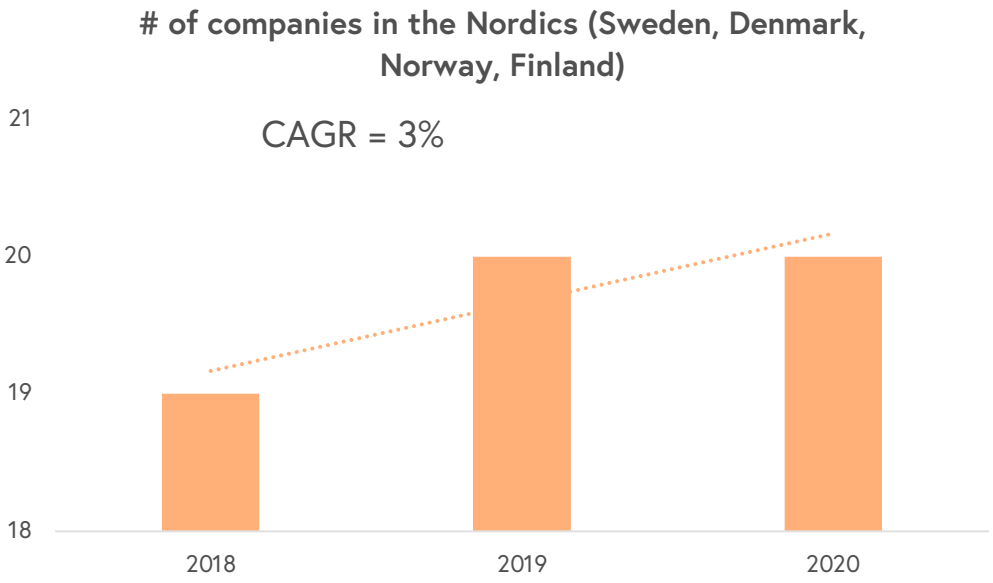


NOTE
The 2020 numbers were taken from the 2020 H1 report and doubled to account for the full year. This might change as the annual report for 2020 is released.

Source: ARM (Alliance for Regenerative Medicine) Global Regenerative Medicine Sector Report: H1 2020 and ARM Annual reports (2017-2019)

Measuring the growth of the ATMP market in terms of growth in number of companies yields a CAGR of 3%

According to this source, the number of ATMP companies in the Nordics grew between 2018 and 2019 but was stagnated between 2019 and 2020.



NOTE
No data set excluding Israel was found. It is not considered to change the CAGR significantly.
The 2020 numbers were taken from the 2020 H1 report and doubled to account for the full year. This might change as the annual report for 2020 is released.

Source: ARM (Alliance for Regenerative Medicine) Global Regenerative Medicine Sector Report: H1 2020 and ARM Annual reports (2017-2019)

On average, it has taken 11.9 years to develop currently approved ATMPs from preclinical stage to first market launch

Drug name	Drug type	Indication	First sign of preclinical development	Preclinical comment	Phase 1 initiation	Phase 2 initiation	Phase 3 initiation	NDA/BLA date	First approval (US/EU)
Kymriah	CAR-T cell therapy	Acute Lymphoblastic Leukemia (ALL)	2007	First mouse model in ALL: Brentjens, R.J. et al. Genetically targeted T cells eradicate systemic acute lympho- blastic leukemia xenografts. Clin. Cancer Res. 13, 5426–5435 (2007).	2012	2014	-	2017	2017
Zolgensma	AAV gene therapy	Spinal muscular atrophy (SMA)	2010	Recieves grant: https://www.curesma.org/zolgensma/	2014	-	2017	2018	2019
Yescarta	CAR-T cell therapy	DLBCL	2009	Kite pharma founded in 2009. Can't find patents before 2014.	2009	2013	2017	2016	2017
Provenge	Autologous cell therapy	Prostate cancer	2000	Mention cancer applications in preclinical for the first time.	-	-	-	2006	2010
Luxturna	AAV gene therapy	Leber congenital amaurosis	2005	Patent mentioning retinitis pigmentosa https://patents.google.com/patent/EP1532246A2/en	2007	2010	2012	2017	2017

	Preclinical	Phase 1	Phase 2	Phase 3
Average time (years)	3,67	2,67	2,5	3
Rounded up time used in calculations (years)	4	3	3	3

NOTE
A conservative approach was adopted by rounding up the average time per phase.

Methodology

Methodology on identifying developing ATMP companies

Methodology

Biomedtracker

- Filtering on industry: biotechnology and gene & cell therapy. Then adding filter on country and phases.
- Using specific country filter and searching through all companies developing biologics for the corresponding country.

Other searches

- Nordic Life Science Database using specific country filter and specific key word searches "cell therapy", "gene therapy" and "tissue engineering"
- Google advanced search using specific country in the "term always included" field and CTMP OR GTMP OR gene therapy OR cell OR "tissue engineering" therapy in the "any of these words" field.
- Identification of tech transfer offices and incubators and adding relevant portfolio companies.

Inclusion criteria

- Companies with development in preclinical to Phase 3, not including international companies that have significant marketing and in-house production.

NOTE
Data was retrieved continuously during Q4 in 2020, and might not be exhaustive and could have changed over time

Methodology on identifying large actors within ATMP

Methodology

- Biomedtracker database (filter on gene & cell therapy, Nordic region)
- Nordic Life Science Database (subsectors: cell therapy, gene therapy, stem cells)
- LinkedIn People search using key words such as gene therapy, cell therapy, CAR-T, tissue engineering, etc. Filter on each country, identify the researchers and their affiliated companies.

Inclusion criteria

- Have marketed products in any pharmaceutical field
- Have R&D function in the Nordic region
- ATMP drug developers (excluding techniques, diagnostics)
- Companies that have international operations

NOTE
Data was retrieved continuously during Q4 in 2020, and might not be exhaustive and could have changed over time

ATMP related universities search strategy

Methodology

- Primary research trough contact with university tech transfer offices.
- Through the Monocl professional platform, MSC identified relevant universities by applying keywords associated with ATMPs (see keywords below) in various compositions.
    - Search strings were constructed on the Monocl platform by using 'Indexed keywords', and the boolean logic was set to 'Preferred'.
    - Primary affiliation was set to 'Academia' to filter on universities.

Keywords in Monocl stakeholder platform

- Mixed search
    - This search was included with a variety of search terms to find the universities that are the most prominent in all ATMP categories compiled and include possible missed universities in tissue engineering.
    - Search terms included: Cell Therapy, Gene expression Monitoring, Gene Action Regulation, Cell Therapy (Historical), Genetic Therapy, Cellular Reprogramming Techniques, Gene Editing, Genetic Engineering, Stem Cells and CAR T-Cell Therapy.
- Gene therapy
    - This search was included to identify universities that are big in gene therapy applications overall.
    - Search terms included: Gene expression Monitoring, Gene Action Regulation, Genetic Therapy, Gene Editing and Genetic Engineering.
- Cell therapy
    - This search was included to identify universities that are big in cell therapy applications overall.
    - Search terms included: Cell Therapy, Cell Therapy (Historical), Cellular Reprogramming Techniques, Stem Cells and CAR T-Cell Therapy.

NOTE
Data was retrieved continuously during Q4 in 2020, and might not be exhaustive and could have changed over time

PubMed publication search strategy

Methodology

- The PubMed search was constructed by the following keyword search strings and conducted for each country according to the country search strings.
- The MeSH heading for CTMP and TEP publications is combined and therefore included.
- Searching strategy for advanced therapies area was combined with the search strategy for country to identify the amount of published research within a country.

Keyword search strings

- **Gene therapy**
  - Search terms included: Gene therapy[MH] OR Genetic Therapy[MH] OR Gene Editing[MH] OR Genetic Engineering[MH] OR Gene Targeting[MH] OR Gene Transfer Techniques[MH] OR Reverse genetics[MH] NOT "CAR-T"[TIAB]
- **Cell therapy and Tissue-engineered products**
  - Search terms included: Cell- and Tissue-Based Therapy[MH] OR cell therapy[MH] OR Cytapheresis[MH] OR Cellular reprogramming [MH] OR "CAR-T"[MH]

Country search string

- Example for Sweden, excluding other countries in the same set: (Sweden[AD] OR Sverige[AD]) NOT ("United Kingdom"[AD] OR UK[AD] OR "Germany[AD]" OR Deutschland[AD] OR Netherlands[AD] OR Holland[AD] OR Nederland[AD] OR Italy[AD] or Italia[AD] OR Denmark[AD] OR Danmark[AD] OR Spain[AD] OR España[AD] OR Espana[AD] OR Norway[AD] OR Norge[AD] OR Finland[AD] OR Suomi[AD])

* [MH]= MeSH Terms, the NLM Medical Subject Headings controlled vocabulary of biomedical terms that is used to describe the subject of each journal article, it is updated annually to reflect changes. [TIAB]=Words and numbers included in a citation's title, collection title, abstract, other abstract and keywords. [AD]=Affiliation may be included for authors, corporate authors and investigators.
** The published research included in this report have publication dates between 2009-01-01 to 2020-11-11

NOTE
Data was retrieved continuously during Q4 in 2020, and might not be exhaustive and could have changed over time

Assumptions on growth and success rate

Methodology

- Publication searches via PubMed and Google searches were done.
- Collection of data from historical Alliance of Regenerative Medicine publications.
- Interviews were held to retrieve more datapoints and anchor previously chosen data points.

NOTE
Data was retrieved continuously during Q4 in 2020, and might not be exhaustive and could have changed over time

www.mscnordics.com

Comments regarding this report can be directed to msc@mscnordics.com