Designing and Manufacturing Medicines with Sustainability at the Core

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Starting with some numbers….

4-5%

Healthcare contribution to global carbon footprint [1]

~10-50%

Due to energy production and consumption [1]

~20%

Of heallthcare foortprint due to disposables [1]

~24 / 124

Kg CO_2e/hr Surgery [2] / Kg CO_2e for a cardiac surgery [3]

7-35%

Of healthcare footprint due to pharmaceuticals [1]

~50%

Adherence to chronic drug regimens [4]

1. Rodriguez-Jimenez et al. 'The Carbon Footprint of Healthcare Settings: A Systematic Review' J. Adv Nurs 2023, **79** 2380
2. Whiting, et al. 'Surgery and the NHS Carbon Footprint' The Bulletin of the Royal College of Surgeons of England Volume 102, Issue 5 July 2020 168
3. Barratt et al. 'Environmental Impact of Cardiovascular Healthcare' Open Heart 2023;10:e002279. doi:10.1136/openhrt-2023-002279
4. Barayokova et al 'Overcoming Barriers to Patient Adherence: The case for developing innovative drug delivery systems' Nature Reviews Drug Discovery | Volume 22 | May 2023 | 387–409 https://doi.org/10.1038/s41573-023-00670-0

Our climate targets

We have set a clear pathway to a net zero impact on climate. By 2030, we aim to reduce carbon emissions by 80% with the remainder offset through investment in high-quality nature-based solutions, and by 2045, we aim to be at the Science Based Target Initiative Net Zero Standard, with carbon emissions reduced by at least 90% and the remainder tackled through high-quality offsets.

2025

100% renewable electricity (scope 2)

2030

80% reduction in carbon emissions and investment in nature-based solutions for the remaining 20% of our footprint (all scopes)*

2045

Net zero emissions across our full value chain by 2045 (all scopes)

- Our net zero targets cover the full value chain of emissions reductions, from a baseline of 2020
- We have re-submitted our new carbon targets and pathway to the Science Based Targets Initiative to verify that they align to a 1.5° pathway, following the demerger of our Consumer Healthcare business
- We have submitted our 2045 target to the Science based Targets Initiative for verification by their Net Zero Standard
- We disclose progress against these targets annually in our Annual Report and ESG Performance Report (2022)

* Previously stated as net zero by 2030, and updated to align with the SBTI Net Zero Standard. See page 16 of the ESG Performance Report for more context

GSK's value chain carbon footprint

Purchased goods and services

Scope 3 emissions from the goods and services that GSK buys from other companies.

3.1m tonnes CO_2e per annum

Purchased goods	1.8m tonnes CO_2e per annum
Purchased services	0.9m tonnes CO_2e per annum
Capital investments	0.2m tonnes CO_2e per annum
Commuting	0.05m tonnes CO_2e per annum
Business travel	0.05m tonnes CO_2e per annum
Upstream energy	0.1m tonnes CO_2e per annum

GSK's operations

Scope 1 and 2 emissions from running our labs, factories and commercial offices.*

0.8m tonnes CO_2e per annum

Energy	0.5m tonnes CO_2e per annum
HFA and manufacturing emissions	0.2m tonnes CO_2e per annum
Sales force	0.1m tonnes CO_2e per annum

* Scope 1 and 2 market-based emissions

Logistics

Scope 3 emissions from delivering medicines and vaccines across the globe.

0.3m tonnes CO_2e per annum

Upstream logistics	0.2m tonnes CO_2e per annum
Downstream logistics	0.1m tonnes CO_2e per annum

Patient use

Scope 3 emissions from patients using our products.

5.1m tonnes CO_2e per annum

Use of metered dose inhalers	5.0m tonnes CO_2e per annum
Use of other products	<0.1m tonnes CO_2e per annum

Disposal

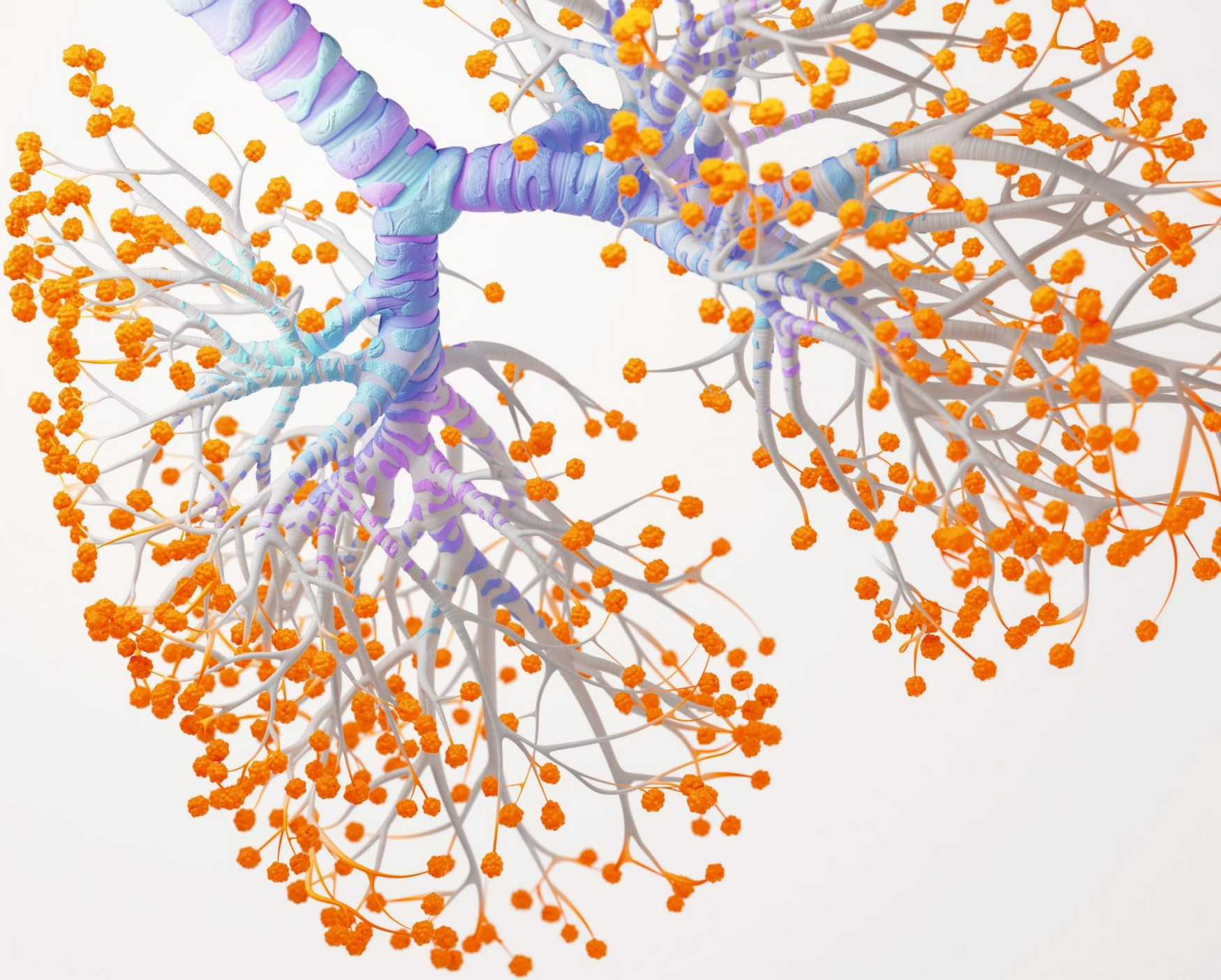
Scope 3 emissions from the disposal of our products by GSK patients.

0.1m tonnes CO_2e per annum

9.39m
Total estimated GSK emissions
tonnes CO_2e per annum*

* based on data from 2021

Asthma



Asthma Treatment

Pre- 2000s

Ventolin CFC

CFC 11/12 Mixtures

~ 100s kg/CO_2e / month

Today

Ventolin HFA
(albuterol sulfate
inhalation aerosol)

HFA-134A

~ 10s kg CO_2e / month

Post 2025?

GSK announces major step towards sustainability ambitions with advancement of low carbon *Ventolin* programme to Phase III trials

- Next-generation propellant technology has the potential to reduce greenhouse gas emissions from *Ventolin* (salbutamol) inhaler by approximately 90%
- Current propellant accounts for 49% of GSK's carbon footprint
- The inhaler is currently prescribed to approximately 35 million patients
- Successful phase III trials to support regulatory submissions in 2025

HFA-152A – potentially single digit kg CO_2e / month

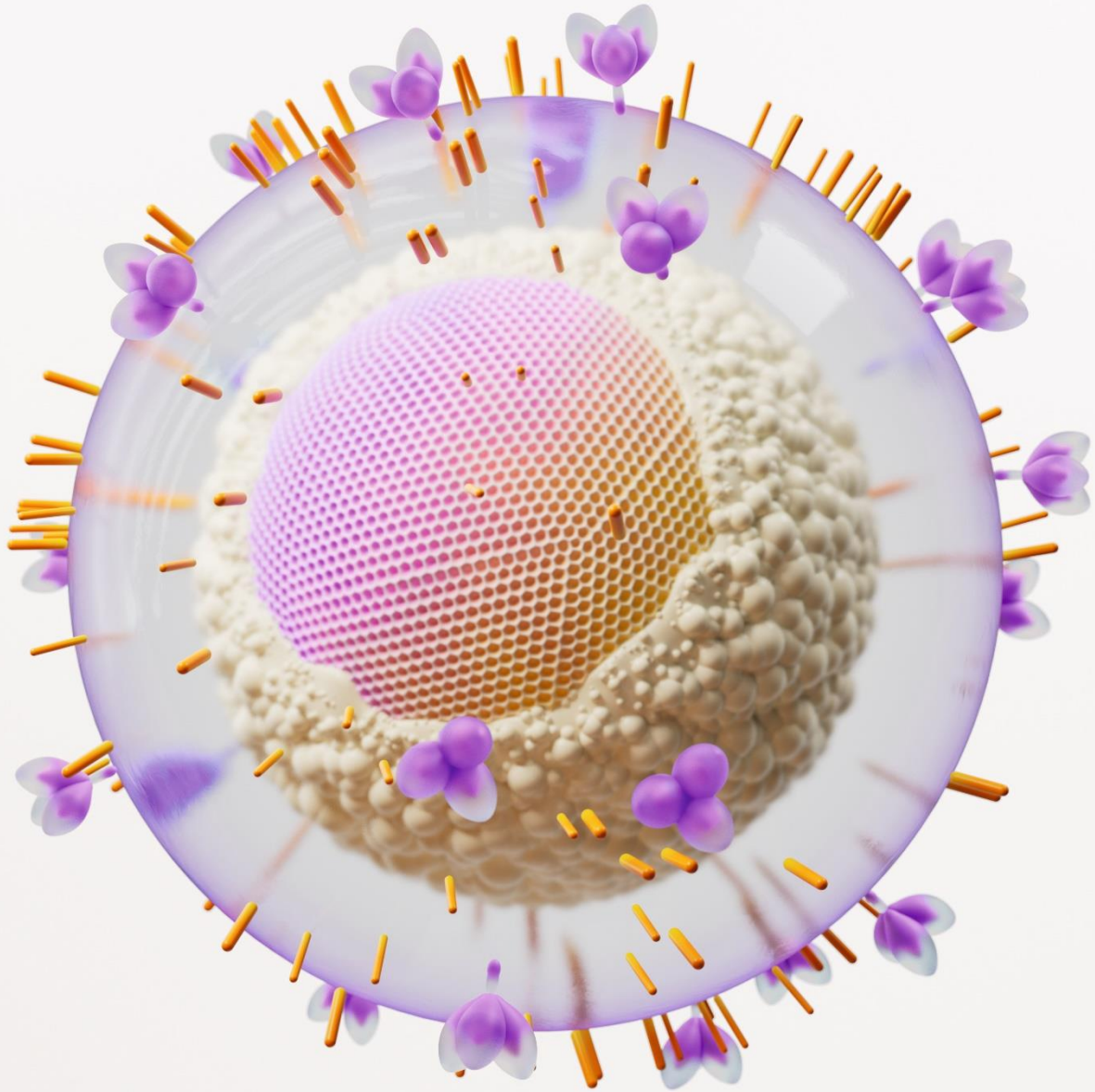
Treatment Approach	Footprint[1]
MDI (HFC gas)	10-36.5 kg CO_2e / month / patient
DPI (no gas)	< 1 kg CO_2e/month /patient

Opportunities

- DPI substitution for MDI where therapeutically possible
- Rapid switch to less impactful MDIs
- Longer acting control therapies

[1]Wilkinson A, Woodcock A. The environmental impact of inhalers for asthma: A green challenge and a golden opportunity. ***Br J Clin Pharmacol***. 2022; 88(7):3016-3022. doi:10.1111/bcp.15135

HIV



Changing the HIV Treatment Paradigm

The benefits of long acting regimens

1990s

~20 tablets /day

2010s – daily fixed dose combinations

2020s – long acting injectables

Future– longer acting Injectables?

Ultra Long Acting

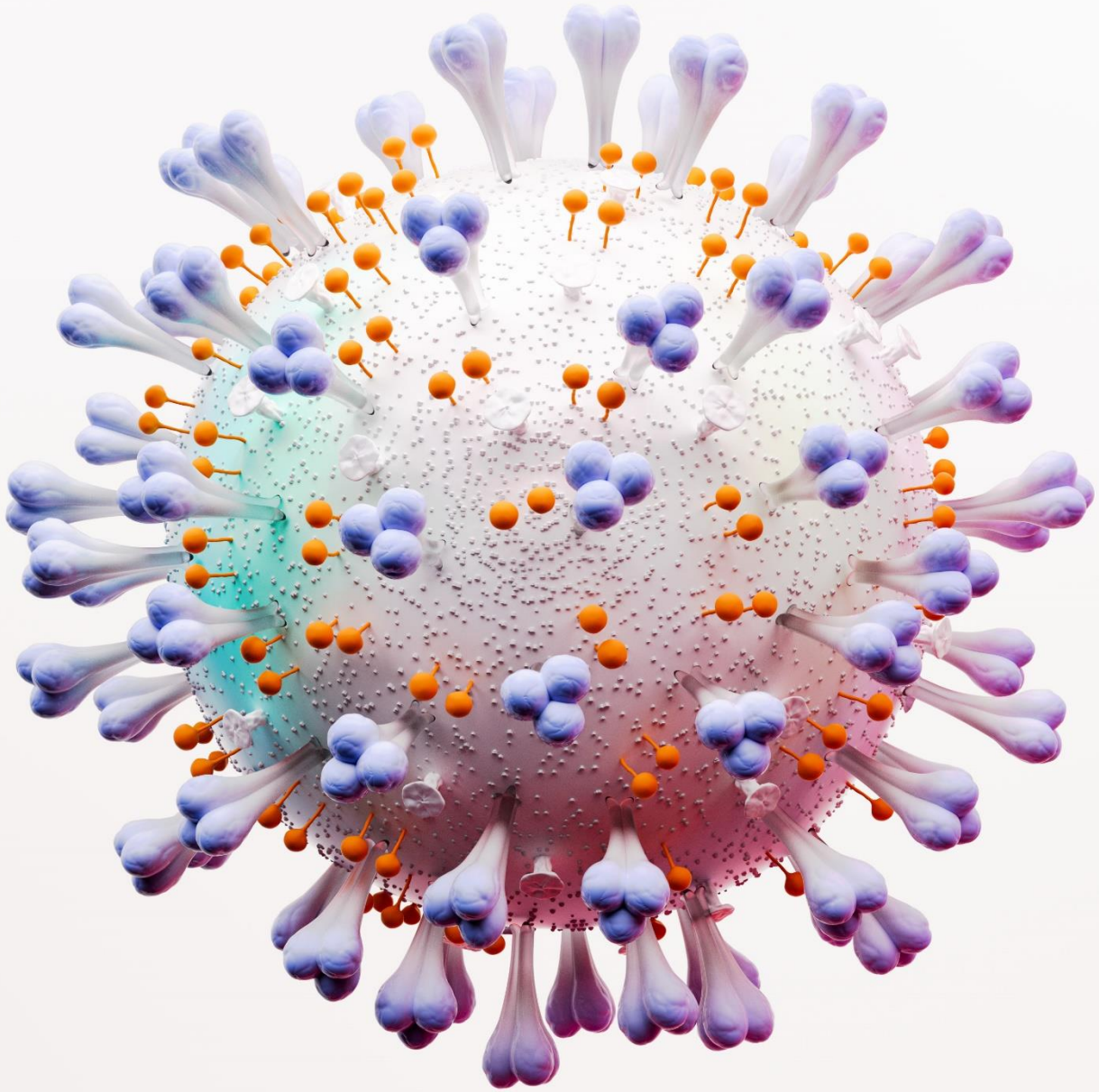
Once / 4 to 6 month dosing

Thousands kg CO_2e/year (up to 20 tablets/day)	Hundreds kg CO_2e/year (one tablet / day)	Tens kg CO_2e/year (6 doses / year)	Approach single digit kg CO_2e/year (2-3 doses / year)

‘98% of people with no previous CABENUVA use preferred injections every other month over daily starter pills, 1% preferred daily starter pills, and <1% reported no preference’

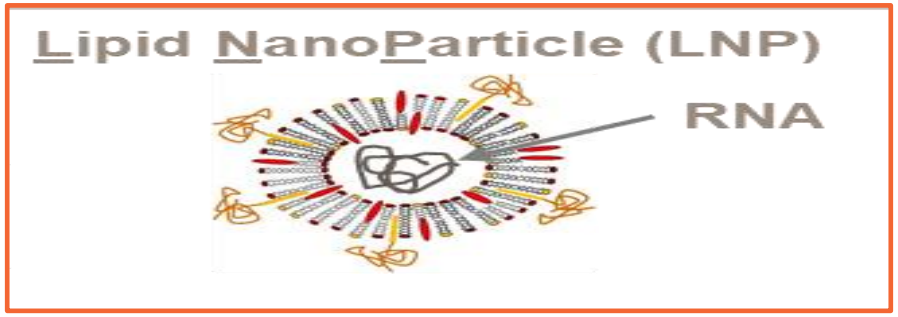
Ref: Clinical Studies | CABENUVA (cabotegravir; rilpivirine)

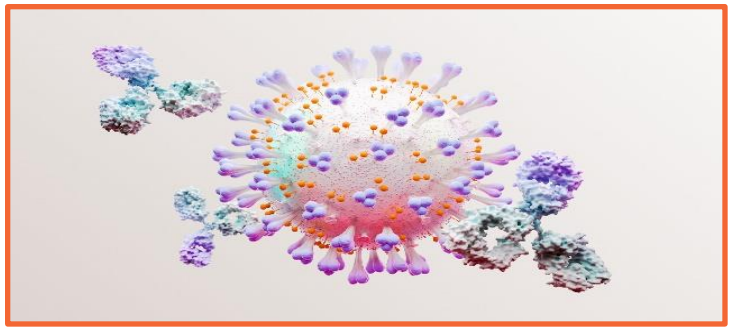
COVID



COVID Therapy Carbon Footprint Paradigms

mRNA therapies offer several opportunities for global footprint reduction





CO_2 estimates for carbon footprint of an mRNA Vaccine[1]

CO_2 Source	% Contribution
Transport (air and ground)	94%
mRNA Process	<< 1%
Packaging (incl glass, syringe, cardboard)	2.9%
Storage (at HCP)	1.4%
Waste (incineration of plastics)	1.7%
Total up to 0.2 kg CO_2 / dose	

Typical mab carbon footprint ranges:

2000 – 10000 kg CO_2 / kg mab[2,3,4]

Covid Antibody Doses: 500 – 1200 mg mab / patient

Carbon footprint of dosing an order of magnitud higher than mRNA dosing -on order of 10 kg CO2e / treatment (not including infusion room energy!)

Future Opportunities

- Combination mRNA vaccines (reduce cold chain costs)
- Thermostable vaccines
- Higher potency mabs with the high process productivities

[1] Int J Environ Res Public Health. 2021 Jul; 18(14): 7425. "The Ecological Footprint of COVID-19 mRNA Vaccines: Estimating Greenhouse Gas Emissions in Germany"

[2].2 Eri Amasawa e al. *ACS Sustainable Chemistry & Engineering* **2021** *9* (42), 14012-14021DOI: 10.1021/acssuschemeng.1c01435

[3] Bunnak et al. 'Life-Cycle and Cost of Goods Assessment of Fed-Batch and Perfusion-Based Manufacturing Processes for mAbs' *Biotechnol. Prog*., 2016, Vol. 32, No.54.

Asthma Pt 2

Eosinophilic Asthma Treatment Paradigms

Pre- 2015

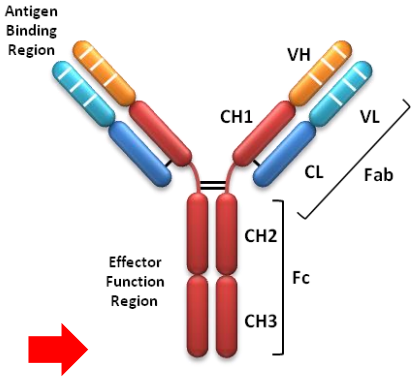
- Corticosteroids
- Long and short acting beta agonists
- Leukotrienes

Current State

Post 2025?

Improved affinity

YTE to extend Serum half-life



Depemokimab (currently in Ph 3 trials)

Multiple once daily

Approaching 1000s kg CO_2e/year

Once per 4 weeks

100s kg CO_2e/year

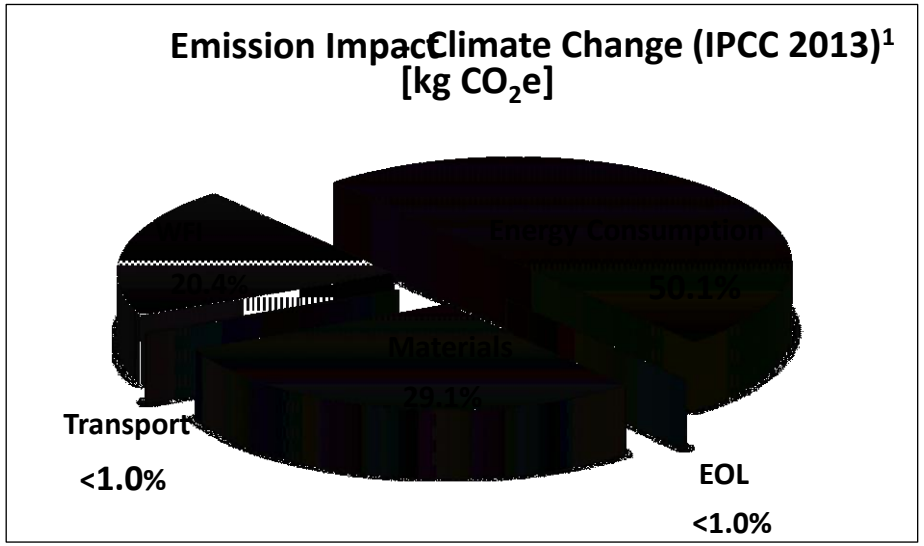
Lifecycle improvements can reduce to 10s kg CO_2e/year

Once per 6 months

Approaching < 10 CO_2e/year order of magnitude

- Future Opportunities
  - Long-acting biologicals that impact a broader range of asthma patients
  - Ambient temperature stability biologics to support this patient class

More on manufacturing….



How to impact energy??

- SUS vs SS?
- Perfusion vs Fed Batch?
- Continuous?

SUB vs SS[2] BUT…. SS would be better if the comparison was 3x 2K SUB vs 6K SS

2K Sub vs 2K SS	% Difference
Ecosystem	~34 (driven by climate change- CIP/SIP, WFI)
Human Health	~32
Resources	~34 (Fossil depletion)

Perfusion vs Fed-Batch

Carbon Footprint
17.4% better for FB (4 day perfusion pooling)
Closer to parity with 8 day pooling period

Continuous vs Batch

Facility Cost – > 60% less (due to footprint)[4,5]
Up to 68% reduction in consumable cost[4]

[1] D'Aquila "An Approach to Ecodesign for Development of more Sustainable Products, Processes, Packaging and Devices, 2023 ISPE Annual Meeting & Expo, October 15-18

[2]. Pieterzykowski, M. et al. "An environmental life cycle assessment comparison of single-use and conventional process technology for the production of monoclonal antibodies" Journal of Cleaner ProductionVolume 41, February 2013, Pages 150-162

3. Bunnak, et al. 'Life-Cycle and Cost of Goods Assessment of Fed-Batch and Perfusion-Based Manufacturing Processes for mAb' Biotechnol. Prog., 2016, Vol. 32, No. 5

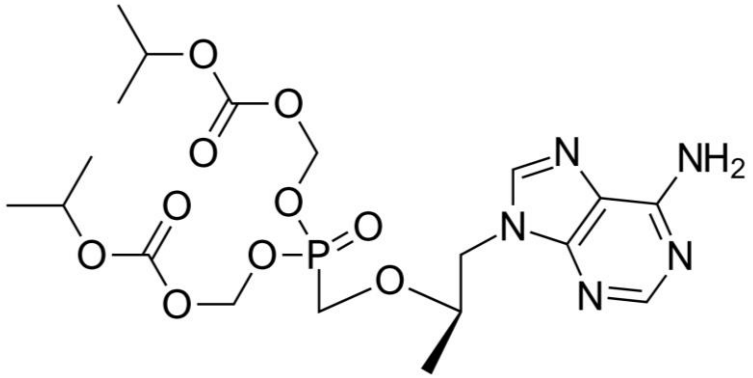
4. Yang, et al. 'Comparison between Batch and Continuous Monoclonal Antibody Production and Economic Analysis' Ind. Eng. Chem. Res. 2019, 58, 5851−5863

5. GSK internal data

Hepatitis B

Hepatitis B Therapy Paradigms

Today

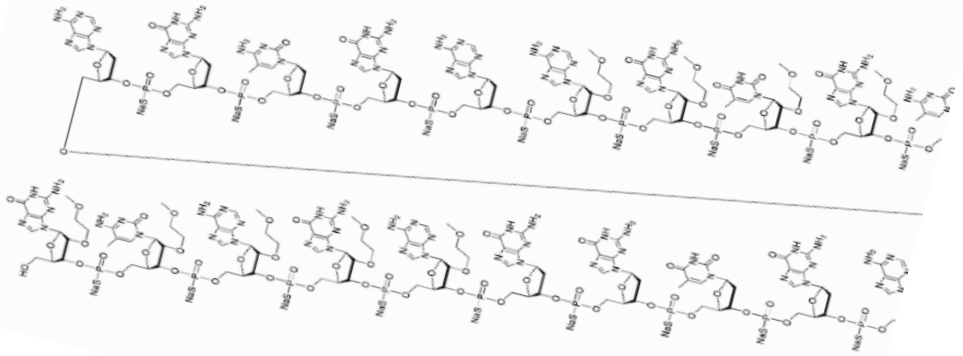


Once daily tenofovir disoproxil fumarate at 245 mg / day

Entecavir once daily at 0.5 mg / day

> 1000 kg CO_2e over 20 years treatment[1]

Post 2025?



Bepirovirsen, approx. 300 mg for 24 weeks, loading dose

100s kg CO_2e for potential treatment regimen

- Future Opportunities
  - Vaccination!!! 2-3 orders of magnitude lower footprint
  - Improvements in oligonucleotide synthesis[2]
  - Improvements in oligonucleotide selectivity / delivery [3]

[1]Tao, et al. Environmental Sustainability of the Globalized Pharmaceutical Supply Chains: The Case of Tenofovir Disoproxil Fumarate *ACS Sustainable Chemistry & Engineering* 2023 *11* (17), 6510-6522DOI: 10.1021/acssuschemeng.2c06518

[2]Sustainability Challenges and Opportunities in Oligonucleotide Manufacturing; Benjamin I. Andrews, Firoz D. Antia, Shawn B. Brueggemeier, Louis J. Diorazio,

[3]Stefan G. Koenig, Michael E. Kopach, Heewon Lee, Martin Olbrich, and Anna L. Watson*The Journal of Organic Chemistry* 2021 *86* (1), 49-61DOI: 10.1021/acs.joc.0c02291

Roberts, T.C., Langer, R. & Wood, M.J.A. Advances in oligonucleotide drug delivery. *Nat Rev Drug Discov* 19, 673–694 (2020). https://doi.org/10.1038/s41573-020-0075-7

Conclusions

- Great progress has been made over the past few decades to improve not just the standard of care but also the carbon footprint of patient therapy
- Prevention always trumps treatment for carbon footprint reduction
  - Vaccines / Long acting medications
- Innovation in medicines for patient benefit nearly always have sustainability benefits
  - Improve adherence
  - Better molecules
- Manufacturing innovations are still required – mab, oligonucleotide, cell therapies
- **Eco-Design benefits not just the environment, but also patients…**

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