The Value of Plasma-Derived Therapies (PDTs): Policies needed to ensure supply to patients & value to society in Greece

Takeda Pharmaceutical Company Limited

Better Health, Brighter Future

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Plasma-Derived Therapies are products that rely on scarce plasma of human donors

Plasma-Derived Therapies are made from humans for humans: their production rely on scarce plasma donations from healthy individuals

Note: Donors are renumerated/reimbursed for the inconveniences caused from donations

Each Plasma-Derived Therapy treated patient needs a large number of plasma donations to provide the amount of product required for their treatment[1]

Amount of plasma donations required to treat one patient for one year

1200 Donations	900 Donations	360 Donations	130 Donations
with **Haemophilia A**	with **Alpha-1** deficiency	with neurologic disorder **(CIDP)**	with **primary immunodeficiency (PID)**

Sources: 1. Jervelund, C., Haanperä, T., Siersbæk, N., The Impact Of Plasma-Derived Therapies In Europe. Copenhagen Economics. June 2021; 1-82

PDT: Plasma-derived Therapies; PID: Primary immunodeficiency disease; CIDP: chronic inflammatory demyelinating polyneuropathy; U.S.: United States

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Plasma-Derived Therapies are critical, life-saving and life-sustaining medicines that treat rare and complex conditions

For many people with rare and complex diseases, plasma therapies are their only treatment option[1,2,3]

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ΑΤΟΜΩΝ ΜΕ ΑΝΑΠΗΡΙΑ (Ε.Σ.Α.μεΑ.)

World Health Organization

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Plasma therapies are named on:

- **World Health Organization's** Model List of **Essential Medicines**[4] &
- **EMA's List of the "Main therapeutic groups" (MTGs) in crisis preparedness**[5]

Letter to MoH August 2023:[6]

ESAMEA named Immunoglobulins as one of the most urgent needs for people with disabilities and chronic conditions in the Health sector in Greece

1) Perez E, et al. J Allergy Clin Immunol. 2017;139(3):s1–s46. 2) Wasserman R, et al. Immunotherapy. 2017;9(12):1035–1050. 3) PPTA. What is Plasma? https://www.donatingplasma.org/donation/what-is-plasma. 4) World Health Organization. WHO Model Lists of Essential Medicines. http://www.who.int/medicines/publications/essentialmedicines/en, 5) https://www.ema.europa.eu/documents/other/list-main-therapeutic-groups-mtgs-crisis-preparedness_en.pdf, accessed Sept 2023, 6) ESAMEA letter to MoH: https://www.esamea.gr/storage/app/uploads/public/64c/b79/645/64cb79645d9bc018399518.docx accessed Sept 2023

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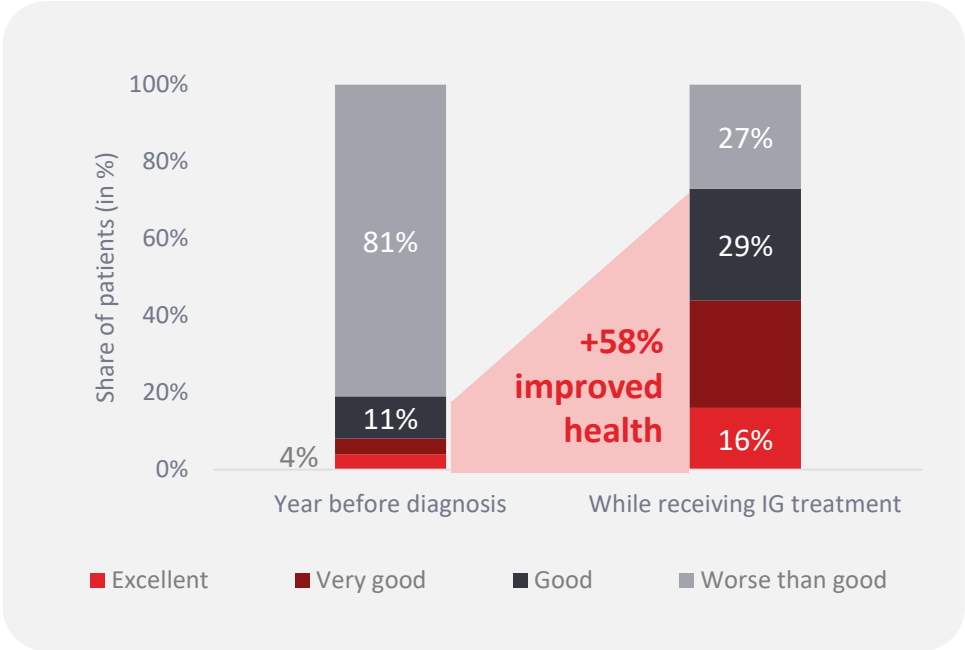
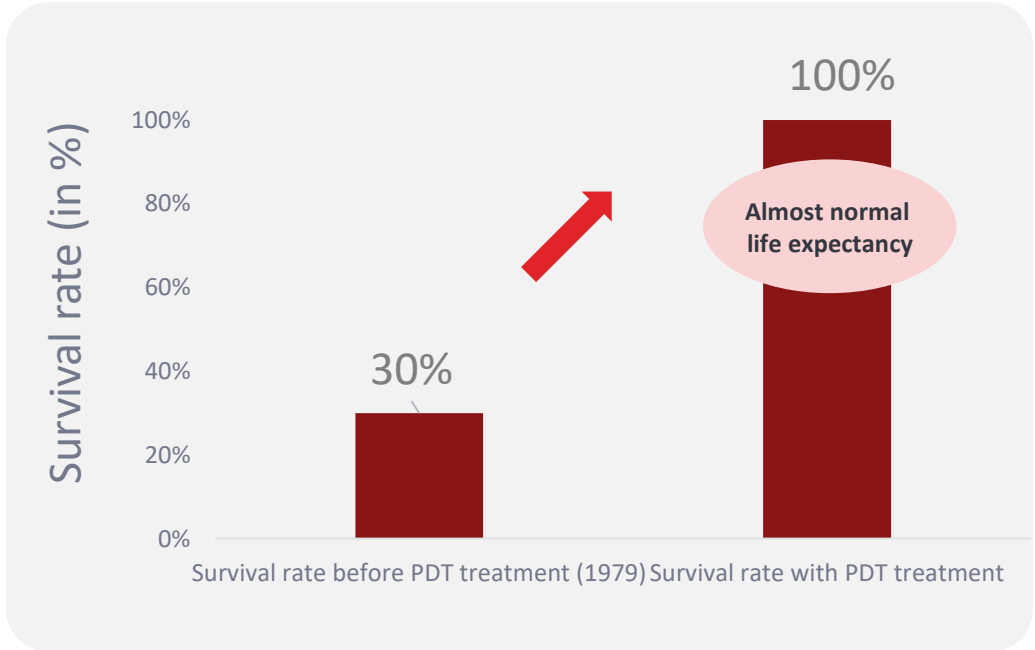
Plasma-Derived Therapies are life-saving treatments and have consistently demonstrated significant clinical and quality of life improvements for patients

Improved self-assessed health for Primary Immunodeficiency Diseases patients[1]



Note: Self-reported health in the year before diagnosis of PID vs.in the year of the study or the last year the patient was receiving IG

Almost normal survival rate for Common variable immunodeficiency patients[2]



Sources: 1. Boyle, M. L., & Scalchunes, C. (2008). Impact of intervenous immunoglobulin (IVIG) treatment among patients with primary immunodeficiency diseases. Pharmaceuticals Policy and Law, 10(1-4), 133-146; 2. Bonilla FA et al: International Consensus Document (ICON): Common Variable Immunodeficiency Disorders. J Allergy Clin Immunol Pract. 2016 Jan-Feb;4(1):38-59

PDT: Plasma-derived therapies; IG: Immunoglobulin; PID: Primary immunodeficiency disease; CVID: Common variable immunodeficiency

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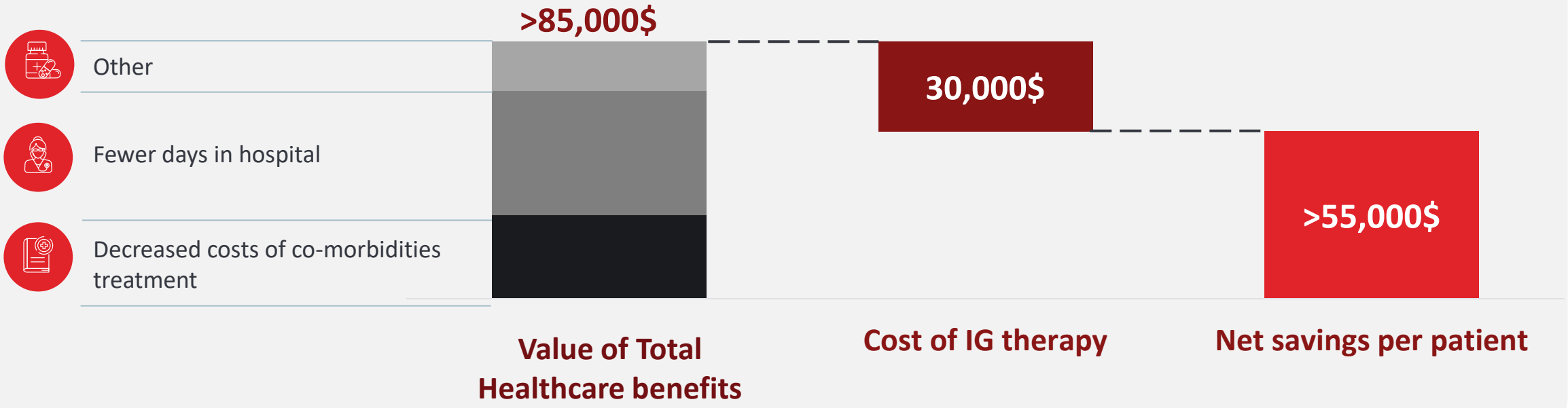
Plasma-Derived Therapies' efficacy in treating patients translates into significant reduction in healthcare expenditures and socio-economic value

Analysis of benefits and costs of treating one Primary Immunodeficiency patient with Immunoglobulins for one year compared to no treatment, in the US [1] :

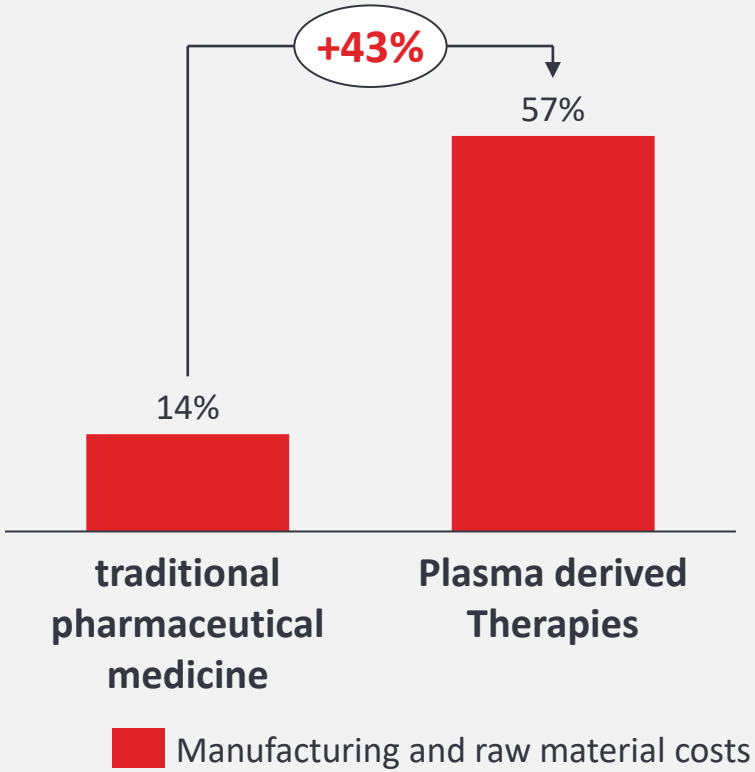


Sources: 1. Modell V, et al. Immunol Res. 2017;65:713-720. Based on US data. Derived by Jervelund C, et al. Copenhagen Economics. 2021 from results in Modell et al. (2017) on the costs of treating a patient with immunoglobulin and the cost of not treating a patient.

IG: Immunoglobulin;

Costs for raw material and Manufacturing costs of PDTs are much higher vs traditional pharmaceuticals[1]

43% higher costs of raw material and manufacturing PDT vs traditional medicine



3-4x longer production times (+6-9 month) for Plasma-Derived Therapies vs traditional pharma

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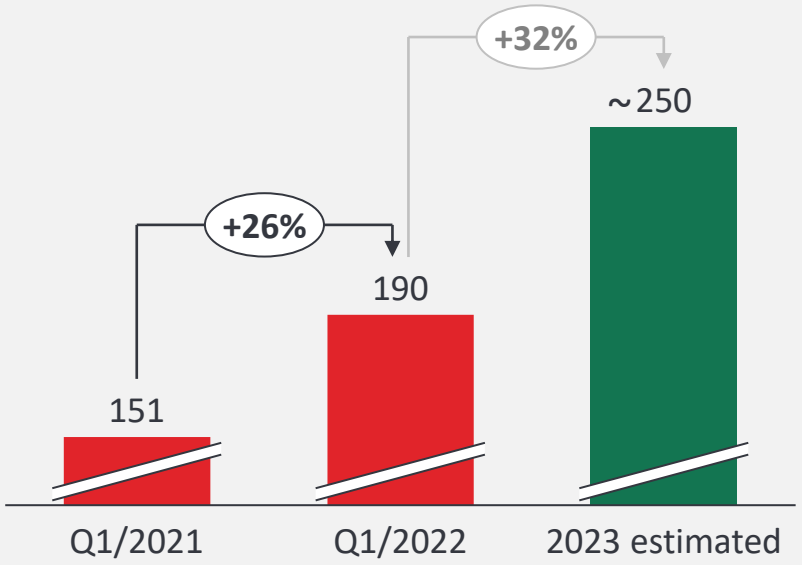
Sources: 1. Kluszczynski et al., (2021) White Paper Key Economic and value considerations for PDMPs Available at: https://www.vintura.com/news/white-paper-key-economic-value-considerations-plasma-derived-medicinal-products-pdmps-europe/

PDT: Plasma-derived therapy

Costs of plasma raw material is high and increasing year on year with a 3-4 times longer manufacturing time vs traditional medicine

High and Increasing cost of source plasma



Cost per liter source plasma in USD[1]

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ESAMEA Letter to MoH August 2023:[2]

"The shortage concerns drugs such as gamma globulin.."

Sources: 1. International Blood/Plasma News. February 2023, Volume 40 Issue 7;
2: ESAMEA: https://www.esamea.gr/storage/app/uploads/public/64c/b79/645/64cb79645d9bc018399518.docx accessed Sept 2023

PDT: Plasma-derived Therapies; UK: United Kingdom

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The growth in demand for PDTs is outpacing the available supply of plasma required to produce them[1]

Immunoglobulins in 19 countries across EU currently on 25th April 2023 with active shortages[4]

>1.000.000

Rare Disease patients across EU can be treated with PDTs[3]

5 million

liters of plasma shortfall in EU[2]

40%

of EU plasma is imported, mainly from US[2]

Sources: 1 World Health Organization. March 2021. https://apps.who.int/iris/bitstream/handle/10665/340171/9789240021815-eng.pdf 2 PPTA. Position Paper on the EU BTC. May 2022. https://www.pptaglobal.org /images/PPTA_Position_paper_on_the_EU_BTC-20May22.pdf 3 Copenhagen Economics, The Impact of Plasma Derived Therapies in Europe, 2021. https://copenhageneconomics.com/publication/ the-impact-ofplasma 4 European Newsletter for Reported Shortages (Q2, 2023) IQVIA

PDT receive list price increases and/or exemption from payback mechanisms in many countries globally to prevent shortages

European Union[1] & the U.K.

17 EU countries increased list price[1] on average over period of 2021-2023 for Kiovig (IVIG) by 33% and/or Hyqvia (SCIG) by 22%

Austria, Cyprus, Croatia, Czech Republic, France, Germany, Hungary, Italy, Latvia, Lithuania, Netherland, Poland, Romania, Slovakia, Spain, Sweden and the UK

Romania[2]

Permanent Exempt all PDTs from payback mechanisms

Belgium[3]

Exempts PDTs from the regular sales tax and from a potential payback tax

Ireland[4]

PDTs exempt from mandatory rebates

Turkey[7, 8]

PDTs are allowed 10% price premium and lower discounted 11% instead of 41%

Portugal[5]

Reduced payback mechanism to PDTs with 2.5% vs 14.3% for other medicinal products

United States[6]

The Inflation Reduction Act, U.S. policymakers exempted PDT to the Medicare price setting provisions

11. Individual national list prices databases available at public domains as a source for the international reference prices 2. Romanian Law no. 340/2018 adopting GEO no. 100/2017 setting financial contributions for financing healthcar https://legislatie.just.ro/Public/DetaliiDocument/231744 3. Belgian Law of 10 June 2006, published on 8 September 2006, reforming contributions on the revenues of reimbursable pharmaceutical products Wet van 10/06/2006 tot hervorming van de heffingen op de omzet van de vergoedbare farmaceutische specialiteiten (openjustice.be) 4. Ireland – The National Centre for Pharmacoeconomics, https://www.ncpe.ie/ 5. Portuguese Law No 82-B/2014 of 31 December, 2015, STATE BUDGET (updated version) https://dre.pt/dre/detalhe/lei/82-b-2014-66016527 6. USA H. R. 5376, 3 January 2022, Inflation Reduction Act https://www.congress.gov/bill/117th-congress/house-bill/5376/text/rh 7. Turkiye Sosyal Güvenlik Kurumu Sağlık Uygulama Tebliği (Social security institution communiqué on healthcare practices) article 4.4.1-(7) https://www.mevzuat.gov.tr/File/GeneratePdf?mevzuatNo=17229&mevzuatTur=Teblig&mevzuatTertip=5 8. Turkiye Beşeri Tıbbi Ürünlerin Fiyatlandırılması Hakkında Tebliğ (Pharmaceutical Products Pricing Communique) Article-9-(1)b link: https://www.mevzuat.gov.tr/mevzuat?MevzuatNo=23924&MevzuatTur=9&MevzuatTertip=5

Review policies like in other countries in Greece to ensure sustainable patient access & supply to essential PDTs

Implement a **differentiated pricing framework** for PDT due to the high and increasing cost of plasma

Review application of **cost containment measures** like clawbacks

Timely **planning on volumes** needed for Greece to ensure sufficient supply with growing demand for PDTs

1) PPTA. The PPTA vision on the plasma protein therapies sector for the next decade in Europe. https://www.pptaglobal.org/images/patientaccess/eu/DGSANCO14003bis_-_PPTA_vision_paper.pdf. 2) IPOPI. PLUS Consensus Principles on Strategies to encourage Blood and Plasma Donations in Europe. https://ipopi.org/wp-content/uploads/2019/02/PLUS-consensus-principles-on-strategies-to-encourage-donations_web.pdf. 3) PPTA. Key Economic and Value Considerations for Plasma-Derived Medicinal Products (PDMPs) in Europe. https://www.vintura.com/wp-content/uploads/2020/03/White-paper-key-economic-and-value-considerations-for-plasma-derived-medicinal-products-PDMPs-in-Europe_Vintura-and-PPTA.pdf.

Policy asks: Introducing policies that encourage plasma donation[1] to ensure sustainable patient access & supply to essential PDTs

- Using **recovered plasma** from whole blood donations for manufacturing PDTs
- Establishing **plasmapheresis infrastructure** & allowing public and private plasma donation infrastructure to co-exist
- Enabling **flexible donation policies** allowing Compensating plasma donors for time and effort expended in donating[2]

1) PPTA. The PPTA vision on the plasma protein therapies sector for the next decade in Europe. https://www.pptaglobal.org/images/patientaccess/eu/DGSANCO14003bis_-_PPTA_vision_paper.pdf. 2) IPOPI. PLUS Consensus Principles on Strategies to encourage Blood and Plasma Donations in Europe. https://ipopi.org/wp-content/uploads/2019/02/PLUS-consensus-principles-on-strategies-to-encourage-donations_web.pdf.

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PDTs present high clinical and socio-economic value for patients and systems that should be recognized by policymakers and payers[1, 2, 3, 4]

Life-saving and life-changing

Cost-effective for health care expenditure

Socio - economic Value

1) PPTA. Key Economic and Value Considerations for Plasma-Derived Medicinal Products (PDMPs) in Europe. https://www.vintura.com/wp-content/uploads/2020/03/White-paper-key-economic-and-value-considerations-for-plasma-derived-medicinal-products-PDMPs-in-Europe_Vintura-and-PPTA.pdf., 2) Jervelund C, et al. Copenhagen Economics. 2021.3) Chapel H, Lucas M, Lee M, et al. Common variable immunodeficiency disorders: division into distinct clinical phenotypes. Blood. 2008; 112(2):277–286. 4) Aledort, L. The evolution of comprehensive haemophilia care in the United States: perspectives from the frontline. Haemophilia. 2016; 22(2):676-683.

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