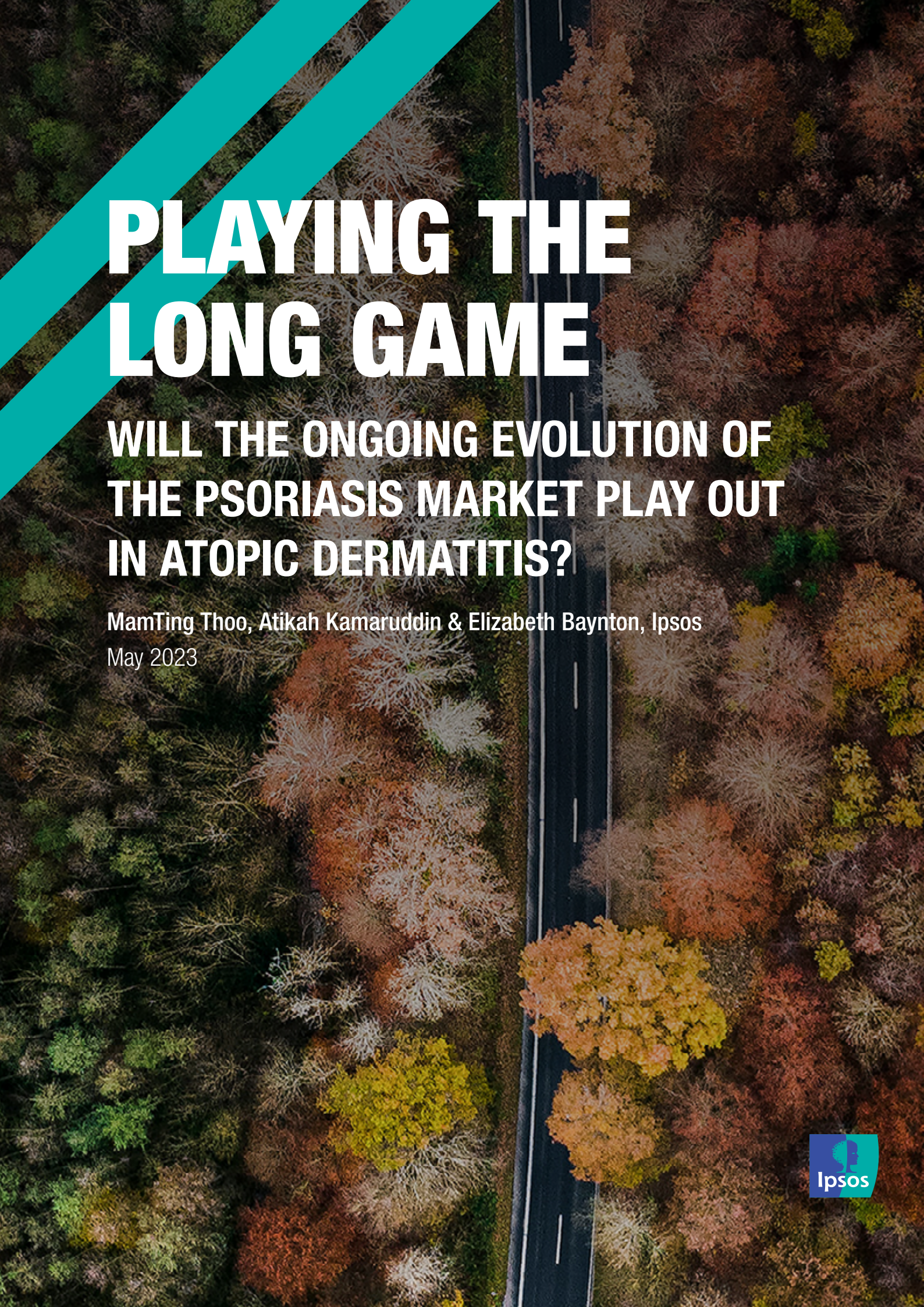

PLAYING THE LONG GAME

WILL THE ONGOING EVOLUTION OF THE PSORIASIS MARKET PLAY OUT IN ATOPIC DERMATITIS?

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Playing the long game: will the ongoing evolution of the psoriasis market play out in atopic dermatitis?

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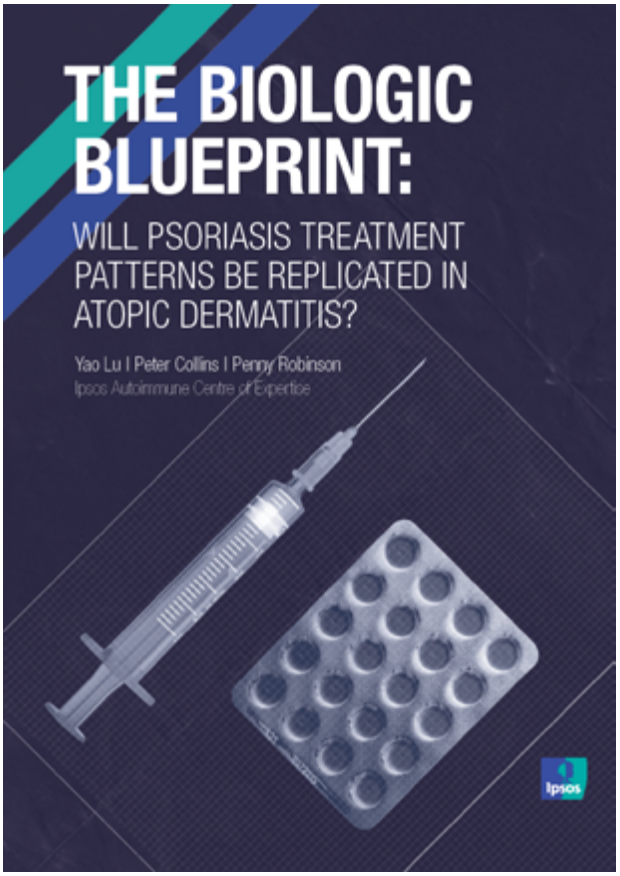

In our 2019 paper, The Biologic Blueprint, we used the psoriasis treatment landscape as a 'proxy' for the AD market, mapping out the evolution of the former as a guide point for what may happen in AD. Four years later we use data from Ipsos' Psoriasis Therapy Monitor* and AD Therapy Monitor* to assess the current state of play: how does the psoriasis market continue to evolve now more therapy classes are available? Did our predictions from 2019 come true? How is the expansion in AD therapeutic options shaping goal setting and expectations in this market, and can we continue to draw parallels between the two conditions?

*See *'About the Research'* for further details

Background

Biologic treatment for moderate-severe psoriasis became possible in 2004, and initially consisted of the tumour necrosis factor inhibitor (TNFi) class. Therapies with alternative mechanisms of action became available from 2009 and expansion has continued, with the advanced therapy treatment landscape now consisting of five therapy classes, all with varying efficacy & tolerability features and modes of administration. In addition, the developmental pipeline for this condition consists of classes with different mechanisms of action again.

Table 1: Advanced therapy classes available to treat moderate – severe psoriasis

THERAPY CLASS	DATE FIRST AVAILABLE IN EUROPE
TNFi	2004[1]
IL-12/23i	2009[2]
PDE-4i	2015[3]
IL-17i	2015[4]
IL-23i	2017[5]

Approval dates based on EMA direction; developmental classes not listed. IL-xxi = interleukin-xx inhibitor; PDE-4i = phosphodiesterase-4 inhibitor

Atopic Dermatitis (AD), another dermatological condition, has been traditionally treated using topical corticosteroids & immunomodulators, UV light therapy and oral medications; the first biologic agent to treat moderate-severe forms of the condition was only made available in 2017. With additional advanced therapy options having since been indicated to treat this condition – with others on the horizon - how is the treatment landscape changing?

Evolution of treatment goals

Given approval times and availability, TNFis understandably dominated the advanced treatment market in psoriasis for many years. Whilst Ipsos' historically trended psoriasis data shows a change in usage of therapy classes as more options are made available, we also see a shift in the importance of treatment goals as perceived by sampled physicians. Back in 2010, when TNFis remained predominant, 75% of sampled physicians perceived that achieving PASI 75 was a key attribute driver for choosing a therapy option; a smaller proportion of the cohort appeared to strive for higher skin clearance levels. Fast forward to 2022, and the need for even greater skin clearance (PASI 90+) has been elevated, as highlighted in figure 1.

FIGURE 1: % sampled physicians citing top 2 box importance of attributes when selecting mod-severe psoriasis treatment

	Q4 2010	Q4 2014	Q4 2018	Q4 2022
Total sampled physicians	**241**	**219**	**230**	**207**
Majority of patients achieve PASI 75 levels of skin clearance	75%	78%	71%	72%
Achieves higher levels of skin clearance (PASI 90 or greater)	65%	77%	78%	82%
Achieves PASI 100 levels of skin clearance			63%	65%

Source: Ipsos Psoriasis Therapy Monitor (Oct – Dec for each of 2010, 2014, 2018 & 2022, ~220 psoriasis-treating physicians per wave across the UK, FR. DE, IT & ES (~equal split across regions) reporting ave. 4 moderate-severe psoriasis patients seen in consultation (variable quota permitted), data collected online. Participating physicians are primary treaters and required to treat a minimum number of psoriasis patients in a typical quarter). Data © Ipsos 2023, all rights reserved.
Top 2 box: sampled physicians who indicated a 6 or 7 rating on a 7-point scale, with 7 being very important. Grey denotes data not captured during this timepoint.

We hypothesise that as additional therapy classes have become available for dermatologists to prescribe - some with higher skin efficacy benchmarks - sampled physicians have higher expectations and heightened treatment goals. We believe this is corroborated when reviewing associations of TNFis versus newer MoA classes with these same therapy drivers over time: the percentage of sampled physicians associating TNFis with high skin clearance levels generally decreases over time. Whilst a higher proportion of the physicians associate IL-17s with higher skin clearance levels versus TNFis in Q4 2018, interestingly this proportion drops for the former therapy class in Q4 2022, possibly as the newer IL-23 class – with its own nuanced efficacy data - becomes more established and expectations once again heighten. [FIG 2].(SEE PAGE 6).

FAST FORWARD TO 2022, AND THE NEED FOR EVEN GREATER SKIN CLEARANCE (PASI 90+) HAS BEEN ELEVATED

FIGURE 2: % sampled physicians associating therapy classes with attributes of mod-severe psoriasis treatment selection

		Q4 2010	Q4 2014	Q4 2018	Q4 2022
	Total sampled physicians	**241**	**219**	**230**	**207**
TNFis	Majority of patients achieve PASI 75 levels of skin clearance	58%	63%	27%	31%
	Achieves higher levels of skin clearance (PASI 90 or greater)	42%	35%	11%	15%
	Achieves PASI 100 levels of skin clearance			8%	9%
IL-17s	Majority of patients achieve PASI 75 levels of skin clearance			47%	48%
	Achieves higher levels of skin clearance (PASI 90 or greater)			47%	40%
	Achieves PASI 100 levels of skin clearance			38%	27%
IL-23s	Majority of patients achieve PASI 75 levels of skin clearance			16%	49%
	Achieves higher levels of skin clearance (PASI 90 or greater)			16%	42%
	Achieves PASI 100 levels of skin clearance			14%	37%

Source: Ipsos Psoriasis Therapy Monitor (Oct – Dec for each of 2010, 2014, 2018 & 2022, ~220 psoriasis-treating physicians per wave across the UK, FR. DE, IT & ES (~equal split across regions) reporting ave. 4 moderate-severe psoriasis patients seen in consultation (variable quota permitted), data collected online. Participating physicians are primary treaters and required to treat a minimum number of psoriasis patients in a typical quarter). Data © Ipsos 2023, all rights reserved.
TNFis = adalimumab (originator and biosimilars), etanercept (originator and biosimilars), infliximab (originator and biosimilars), golimumab and certolizumab pegol; IL-17is = secukinumab, ixekizumab, brodalumab, bimekizumab; IL-23is = guselkumab, tildrakizumab, risankizumab. Grey denotes data not captured during this timepoint.

Given that treatment goals have seemingly evolved in psoriasis following the embedding of additional treatment options, do we see a similar pattern in AD?

Not quite. Or maybe, there hasn't been enough time yet. When reviewing the proportion of physicians in our AD Therapy Monitor between 2020 and 2022 who deem specific therapy drivers to be important, there are few 'stand-out' drivers that show a more obvious increase (or decrease) in importance, like we saw in our psoriasis data. Admittedly, based on data availability, we are looking at a much more condensed timespan [FIG 3].

FIGURE 3: % sampled physicians citing top 2 box importance of attributes when selecting mod-severe AD treatment

	Q4 2020	Q4 2021	Q2 2022
Total sampled physicians	**217**	**211**	**230**
Substantially improves patient quality of life	86%	79%	81%
Provides good overall efficacy	81%	76%	78%
Reduces frequency/severity of flares	79%	71%	78%
Relieves itching	76%	75%	77%
Addresses the pathophysiology of type II inflammation	46%	48%	57%

Source: Ipsos Atopic Dermatitis Therapy Monitor (Oct – Dec 2020, Oct – Dec 2021, Apr – Jun 2022, ~220 AD-treating physicians per wave across the UK, FR. DE, IT & ES (~equal split across regions) reporting ave. 4 moderate-severe AD patients seen in consultation (variable quota permitted), data collected online. Participating physicians are primary treaters and required to treat a minimum number of AD patients in a typical quarter).
Top 2 box: sampled physicians who indicated a 6 or 7 rating on a 7-point scale, with 7 being very important.

What we do see is a dip in perceived importance between 2020 and 2021, which then rises again in 2022, for some key drivers such as efficacy and relieving itching. It could be that an uptick in importance in physicians' minds is taking place now that more treatment options are becoming available in AD. It is worth monitoring this possible shift and if they increase in importance further as new MoAs entrench. "Addressing the pathophysiology of type II inflammation" is also an attribute of seemingly higher importance over time, suggesting niche efficacy benchmarks of AD therapies may shape the aim of treatment going forward.

That being said, when sampled physicians reporting on AD patients were specifically asked their top three treatment goals for each patient they submitted a record for, objectives did appear to centre more on enhancing quality of life and a longer-term, holistic outcome versus specific skin-oriented gains, whereas we saw psoriasis to be more skin-focused [FIG 4].

FIGURE 4: % Reported mod-severe AD patients with treatment goals specified by sampled physicians

	Q2 2020	Q4 2020	Q4 2021
Total reported AD patients	**1019**	**1089**	**1113**
Improve patient's quality of life	67%	51%	51%
Disease control over the long term		39%	40%
Symptomatic control		34%	35%
Appease patient's itch	56%	38%	36%
Improve skin appearance quickly	32%	17%	19%
Lower patient's EASI score	16%	11%	12%

Source: Ipsos Atopic Dermatitis Therapy Monitor (Apr – Jun 2020, Oct – Dec 2020, Apr – Jun 2021, ~220 AD-treating physicians per wave across the UK, FR. DE, IT & ES (~equal split across regions) reporting ave. 4 moderate-severe AD patients seen in consultation (variable quota permitted), data collected online. Participating physicians are primary treaters and required to treat a minimum number of AD patients in a typical quarter). Data © Ipsos 2023, all rights reserved. Grey denotes data not captured during this timepoint.

The elephant in the room: safety

A key factor we feel needs to be addressed and may be influencing nuances in the AD treatment market is that of safety. Many new advanced therapy options made available in AD over the last few years are JAK inhibitors, a therapy class required to carry boxed warnings concerning potential side effects and associated risk factors when using them.

"CONCERNS ABOUT SIDE EFFECTS" WAS CONSIDERED THE TOP REASON FOR NOT PRESCRIBING A JAK INHIBITOR TO REPORTED AD PATIENTS

Whilst our psoriasis data showed certain molecules to be associated with a favourable side effect profile and established long-term safety (as well as efficacy factors), which may have helped carve a niche in the treatment landscape, some new treatments in AD may not be afforded such grace right now. “Concerns about side effects” was considered the top reason for not prescribing a JAK inhibitor to reported AD patients in our Q4 2021, Q2 2022 and Q4 2022 AD Therapy Monitor data, despite sampled physicians deeming them eligible for one.

In our 2019 PoV, we predicted that existing biologic share in AD will be heavily challenged with the approval of the new advanced therapies. We are yet to observe such shifts in our data, possibly due to a combination of newer therapies still establishing themselves, and the influence of aforementioned risk factor considerations. Instead, greater impact has so far been seen on less targeted treatments, such as traditional immunosuppressants.

Conclusion

Four years on from our last opinion piece, it is apparent that treatment goals have become honed, and expectations are higher among psoriasis treaters in our sample. Therapy classes with alternative mechanisms of action have possibly raised the efficacy bar: more is expected from treatment and the advanced therapy landscape has become increasingly more goal-oriented and nuanced.

AD’s advanced therapy landscape is still in relative infancy by comparison. Perceived treatment goals of treaters in our sample still appear to be in flux and centred around more holistic, less specific quality of life factors. It is also a treatment environment potentially more conscious of safety parameters that psoriasis did not have to contend with. That being said, there does appear to be opportunity for newer advanced therapies to take the place of more traditional, less specific therapies.

The introduction of new targeted therapy options to the AD armamentarium may take some time to elicit change in the therapeutic landscape. In which case, their impact may not manifest in the same way – or to the same degree – as that seen in psoriasis.

In AD, those in the industry may have to be mindful of playing the long game.

About the Research

The Ipsos Psoriasis Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of biologic/targeted oral treatment for moderate-severe psoriasis patients. Participating physicians are screened for specialty, number of psoriasis patients seen in a typical three-month period and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of psoriasis patients seen in consultation, and responses to a perceptual questionnaire (once per year). Data used in this article were collected online. Sample sizes are provided alongside the relevant charts.

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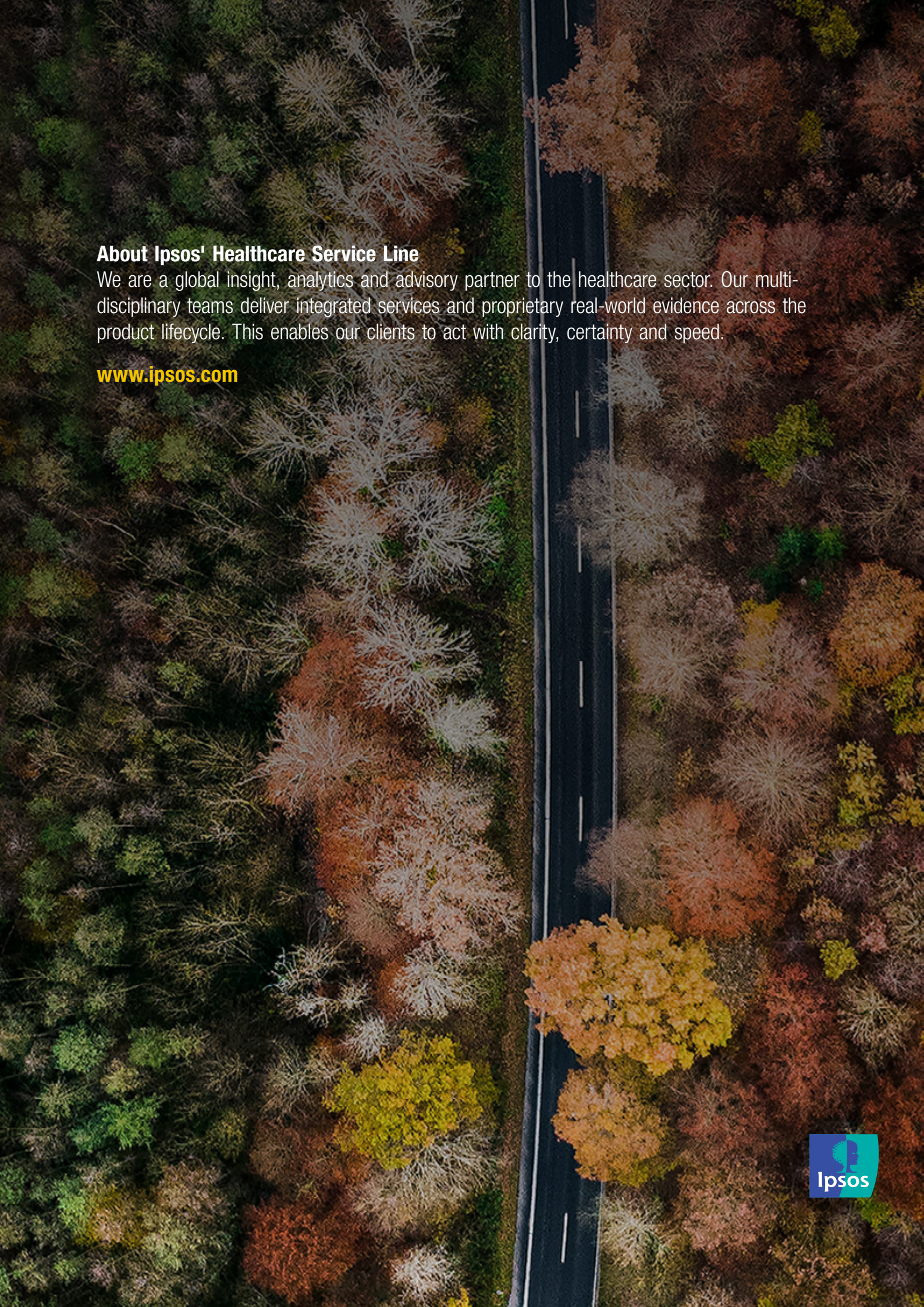

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