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BiondVax Pharmaceuticals, Ltd. (BVXV-NASDAQ)

BVXV: Phase 3 Data for Universal Flu Vaccine in Late September to Late October 2020…

Based on our probability adjusted DCF model that takes into account potential future revenues from M-001 as a universal flu vaccine, BVXV is valued at $81/share. This model is highly dependent upon continued clinical success of M-001 and will be adjusted accordingly based upon future clinical results.

OUTLOOK

BiondVax Pharmaceuticals, Ltd. is a biopharmaceutical company developing a universal influenza vaccine (M-001) designed to protect individuals from all strains of influenza. The company is currently conducting a pivotal Phase 3 clinical trial of M-001 in a total of approximately 12,400 adult volunteers aged 50+ (with half aged 65+) with results expected in late September to late October 2020.

Current Price (08/31/20)	$36.01
Valuation	**$81.00**

SUMMARY DATA

52-Week High	**$51.10**
52-Week Low	**$5.36**
One-Year Return (%)	**510.34**
Beta	**2.32**
Average Daily Volume (sh)	**61,928**
Shares Outstanding (mil)	**11**
Market Capitalization ($mil)	**$409**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**4**
Insider Ownership (%)	**6**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2020	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
2021					0.0 E
2022					45.0 E

Earnings Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.01 A	-$0.05 A	-$0.02 A	-$0.03 A	-$0.09 A
2020	-$0.00 A	-$0.03 A	-$0.01 E	-$0.01 E	-$0.06 E
2021					-$0.06 E
2022					-$0.03 E

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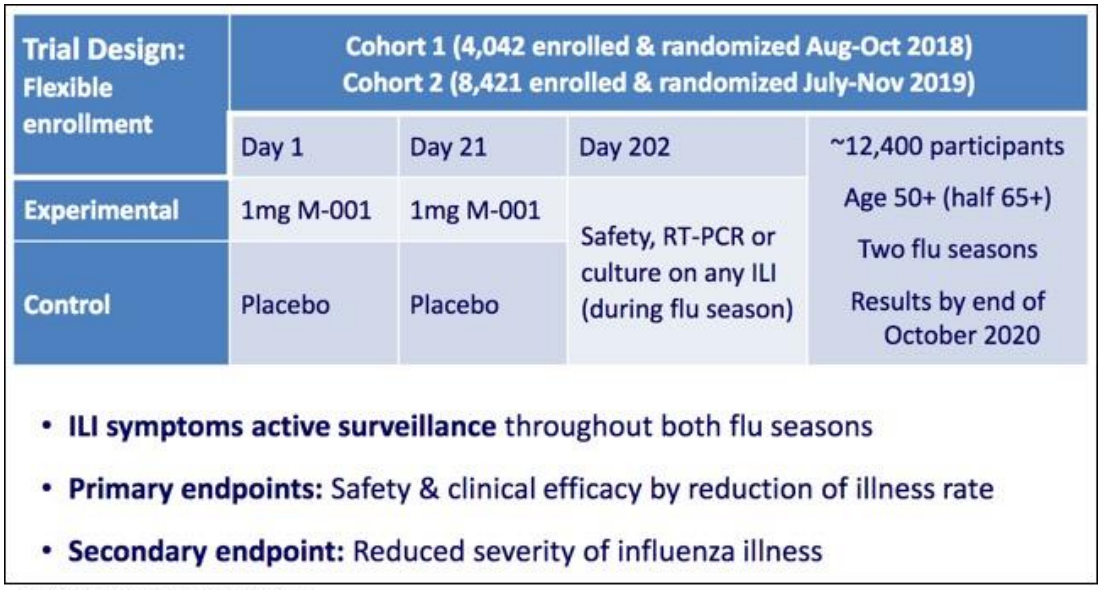
WHAT'S NEW

Business Update

M-001 Phase 3 Results in Late Sep. to Late Oct.

BiondVax Pharmaceuticals, Ltd. (BVXV) is a biopharmaceutical company developing a universal influenza vaccine (M-001) designed to protect individuals from all strains of influenza. The company's strategy for commercializing M-001 involves testing it in a pivotal Phase 3 program as a standalone influenza vaccine to assess its clinical efficacy. The ongoing Phase 3 trial is being conducted in Europe following feedback about the trial design and approval to initiate it from the European Medicines Agency (EMA). The EMA also stated that "a single pivotal efficacy trial that provides a robust demonstration of efficacy against laboratory-proven influenza like illness (ILI) could suffice for an approval".

In August 2020, the company announced that the results from the Phase 3 trial are anticipated in late September to the end of October 2020 based on the current operational activities. The trial enrolled a total of approximately 12,400 adults aged 50 years and older (approximately half were 65+) that were randomly assigned to receive either M-001 or placebo with 4,042 enrolled in Cohort 1 and dosed prior to the 2018/2019 influenza season and 8,421 enrolled in Cohort 2 prior to the 2019/2020 influenza season. The primary outcome of the trial is safety and reduction of illness rates. All participants were monitored for influenza-like illness (ILI) symptoms throughout the influenza season and swabs were collected from any participant with ILI symptoms and influenza infection confirmation was conducted by a qualified laboratory. In addition, cell-mediated immunogenicity markers of M-001 are being evaluated in a subset of participants. An overview of the trial is given below.



Source: BiondVax Pharmaceuticals Ltd.

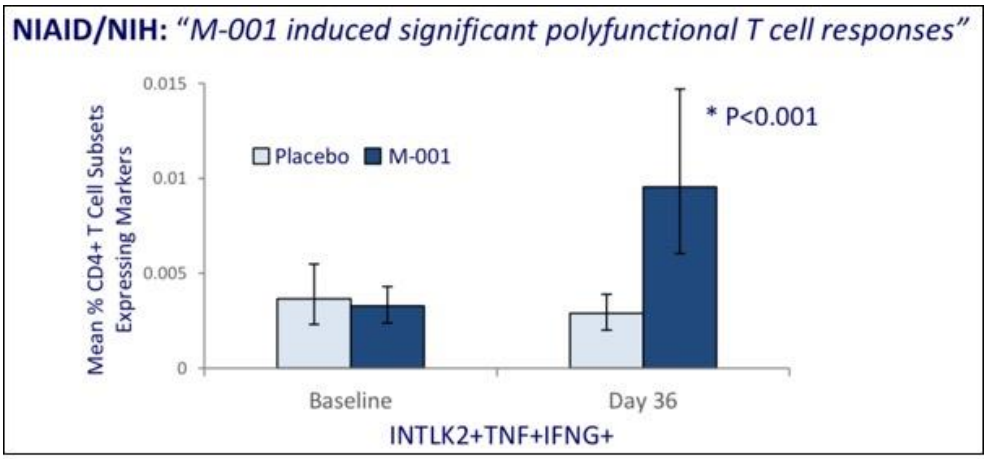
Laboratory analysis of specimens collected from any study participants presenting with ILI have been completed for the first cohort of 4,094 participants. Of those 4,094, a total of 1,135 ILI cases were reported and of those there were 137 laboratory confirmed influenza cases. The trial remains blinded, so we will not know how those cases were distributed between those receiving M-001 and placebo until the topline results are released, however it is important to note that there have been no treatment related safety concerns.

While the development of M-001 is not directly related to the current coronavirus outbreak, what the COVID19 pandemic shows is that an effective universal influenza vaccine could help to alleviate the overall burden on healthcare systems around the world, thereby making it easier to handle novel viral outbreaks, such as SARS-CoV-2. In the current environment, an effective universal influenza vaccine could both reduce the number of individuals experiencing influenza-like illnesses, thus making it easier to identify those suffering from the novel coronavirus, and reduce the rates of hospitalization for those suffering from influenza, thus freeing up valuable hospital resources.

Primary Endpoints Achieved in Phase 2 Trial of M-001

On June 10, 2020, BiondVax announced the completion of the study report for the Phase 2 clinical trial of M-001 sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH) and conducted by NIAID Vaccine Treatment and Evaluation Units. The study results can be found here. The trial enrolled 120 participants between the ages of 18-49 at three centers in the U.S. Each participant received two doses of M-001 in the Spring and then a dose of the seasonal quadrivalent influenza vaccine in the Fall. The length of time between immunizing with M-001 and the seasonal influenza vaccine was much longer in this trial (~ six months) compared to approximately three weeks in previous trials. The primary objectives of the trial were to assess the safety of M-001 and the T cell responses to M-001 component peptides. Secondary objectives of the trial included assessing serum antibody responses to the seasonal influenza vaccine target viruses.

The results of the trial showed that M-001 was safe and well tolerated and induced significant polyfunctional T cell responses, which is in line with the six previously completed clinical trials of M-001. The following graph shows one of the positive endpoints, with patients immunized with M-001 and the seasonal quadrivalent influenza vaccine showing a statistically significant increase in the percentage of CD4+ T cells that express interleukin 2 (INTLK2), tumor necrosis factor (TNF), and interferon gamma (IFNG) compared to those administered only the seasonal quadrivalent influenza vaccine. We anticipate the full results being published in a peer-reviewed journal later this year.



Source: BiondVax Pharmaceuticals, Ltd.

The positive results from this trial are all the more encouraging given the fact that it was conducted independently by the NIH. BiondVax supplied M-001 and contributed to the design of the study, however the NIH sponsored, conducted, and performed all data analysis. We also believe it is important to note that the principal investigator of the trial, Dr. Robert Atmar, is currently serving on the Advisory Committee on Immunization Practices (ACIP), which is a 15-member board that is responsible for making vaccine recommendations to the Director of the Centers for Disease Control (CDC) regarding the use of vaccines for effective control of vaccine-preventable diseases in the civilian population of the U.S.

Financial Update

On August 20, 2020, BiondVax announced financial results for the second quarter of 2020. As expected, the company did not report any revenues during the second quarter of 2020. R&D expenses in the second quarter of 2020 were approximately $3.4 million compared to approximately $7.9 million in the fourth quarter of 2019. BiondVax exited the second quarter of 2020 with approximately $11.2 million in cash and cash equivalents. In May 2020, the company announced the receipt of approximately $4.2 million since Jan. 1, 2020 through the exercise of warrants. The publicly traded warrants (BVXVW) had an exercise price of $6.25 and expired May 15, 2020. We estimate that BiondVax now has sufficient capital to fund operations at least through the end of 2020, and importantly past the release of topline data from the Phase 3 study of M-001.

BiondVax now has approximately 11.4 million ADSs outstanding and when factoring in stock options a fully diluted ADS count of approximately 12.0 million.

Background on M-001

BiondVax is developing the M-001 vaccine, a synthetic peptide-based protein that targets both existing and future seasonal and pandemic strains of the influenza virus. The vaccine targets conserved regions of Type A and B influenza viruses such that M-001 could be considered a "universal" influenza vaccine, capable of offering immunological protection against all strains of the influenza virus.

M-001 is composed of nine peptides that are believed to be common to most known influenza strains in existence, in part because these peptides seem to be critical for the virus' ability to infect a host cell. They are derived from hemagglutinin (HA), matrix 1 (M1) and nucleoprotein (NP) viral proteins and are arranged as triplicates into a single recombinant protein easily manufactured in bacteria. HA is an antigenic glycoprotein found on the surface of influenza viruses and is also the main constituent for a number of seasonal influenza vaccines. However, the peptides from HA in M-001 are derived from the inner parts of the protein where little to no variability between strains exists. M1 is a matrix protein that forms a layer under the patches of the viral cell membrane that contain HA, NA, and M2 proteins, and is responsible for mediating the encapsulation of RNA-nucleoprotein complexes into the membrane envelope (Sha *et al*., 1997). NP is a structural protein that encapsidates the viral RNA inside the virus. The sequence of each of the peptides is shown below, along with the order in which the peptides are arranged in the full-length recombinant protein.

Peptide	Amino Acids Sequence
Hemagglutinin (HA) epitope 1	PKYVKQNTLKLAT
Hemagglutinin (HA) epitope 2	SKAYSNCYPYDVPDYASL
Hemagglutinin (HA) epitope 3	WLTGKNGLYP
Hemagglutinin (HA) epitope 4	WTGVTQN
Hemagglutinin (HA) epitope 5	PAKLLKERGFFGAIAGFLE
Nucleoprotein (NP) epitope 6	FWRGENGRKTRSAYERMCNILKGK
Nucleoprotein (NP) epitope 7	SAAFEDLRVLSFIRGY
Nucleoprotein (NP) epitope 8	ELRSRYWAIRTRSG
Matrix (M) epitope 9	SLLTEVETYVP

(HA epitope 1) - (HA epitope 2) - (M1 epitope 9) - (HA epitope 3) - (HA epitope 4) - (NP epitope 6) - (HA epitope 5) - (NP epitope 7) - (NP epitope 8).

Source: Atsmon *et al*., 2012

The peptides were selected based upon their ability to elicit either a B- or T-cell immune response and each of them has the ability to bind to a wide array of human leukocyte antigen (HLA) proteins (both Class I and Class II), which are responsible for presenting peptides to the immune system. Some may question the use of peptides from proteins located inside the virus, however there is a strong rationale for their use. It has long been known that a mild influenza infection in animals provides protection against a subsequent, more severe challenge with a virus harboring different HA and NA (Yetter *et al*., 1980). This effect appears to be mediated by both CD4+ and CD8+ T-cells that recognize conserved regions on viral proteins (Furuya *et al*., 2010). The CD4+ T-cells that are specific for conserved internal viral antigens also potentiate antibody responses to the HA of subsequently encountered viruses (Scherle *et al*., 1986). The end result is that immunizing with conserved internal viral antigens results in an increased immunological response to infection following subsequent exposure to influenza viruses.

Previous Clinical Trial Results

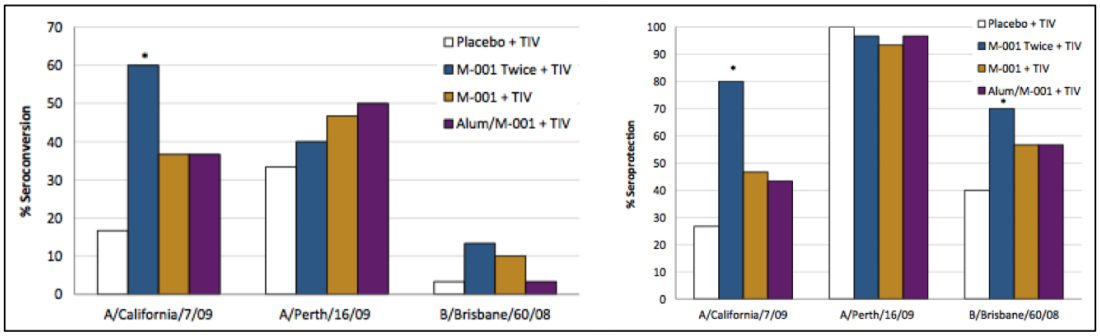
M-001 had been tested in 698 participants through six different clinical trials, with the details presented in the following chart. In each of the trials, the vaccine was shown to be safe and able to induce a robust immune response.

Phase	Trial	Year	Population (age)	Total Participants	Status	Results
1/2	BVX-002	2009	Younger Adults (18-49)	63	Completed	M-001 was well tolerated and a cellular (CMI) and humoral (priming effect) immune response was observed
1/2	BVX-003	2010	Older Adults (55-75)	60	Completed	
2	BVX-004	2011	Younger Adults (18-49)	200	Completed	
2	BVX-005	2012	Elderly (65+)	120	Completed	
2	BVX-006	2015	Older Adults (50-65)	36	Completed	
2b	BVX-007*	2015-16	EU Adults (18-60)	219	Completed	

Source: BiondVax Pharmaceuticals Ltd.

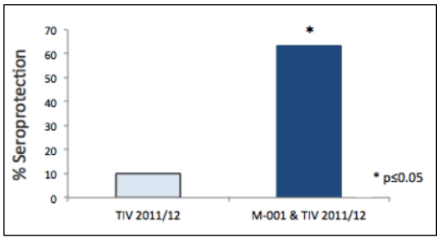
BVX-002 (Atsmon *et al.*, 2012): This was a single-center, randomized, placebo controlled, single blind first-in-human study to examine the safety and immunological response to M-001 in healthy adults age 18-49. For safety purposes, three subjects were dosed once with 0.125 mg of M-001 and monitored for 7-9 days before the rest of the patients were administered the planned doses. There were four dosing cohorts, and within each cohort subjects were randomized in a 2:1 fashion to receive either 0.25 mg or 0.5 mg M-001 (n=10) or placebo (n=5), with or without adjuvant. The results showed that M-001 was well tolerated with only mild and moderate adverse events (AEs), with no significant difference between vaccine and placebo recipients for AEs. A robust humoral (antibodies to M-001) and cellular (PBMC proliferation to viral peptides) immune response was noted for participants immunized with M-001, and while there were greater humoral responses in patients immunized with M-001 plus adjuvant, there did not appear to be a difference in cellular response between subjects dosed with adjuvant and those without.

BVX-005 (Atsmon *et al.*, 2014): This was a two-center, randomized, placebo controlled study in a total of 120 elderly volunteers (age 65+). The subjects were randomized 1:1:1:1 into four parallel groups to receive either 1) two sequential non-adjuvanted 0.5 mg M-001, or 2) a single non-adjuvanted 0.5 mg M-001, or 3) a single adjuvanted IM injection of 0.5 mg M-001, or 4) one placebo injection. All participants subsequently received the seasonal trivalent influenza vaccine (TIV) three weeks following the last M-001 or placebo injection. The primary outcome measures were safety, tolerability, and tolerance of M-001 with secondary outcomes being humoral and cellular immune responses. The results showed that priming with M-001 enhanced seroconversion towards all three strains in that season's influenza vaccine (denoted on the y-axis in the figure below). The following figure shows the percentage of patients that tested positive for seroconversion (defined as a mean fold increase in anti-HA antibody levels of ≥ four-fold from levels detected in sera collected on day 0, and reaching a level of ≥1:40 post-immunization) and seroprotection (defined as the number of participants per cohort expressing anti-HA antibody levels of ≥1:40 post-immunization). Addition of an adjuvant did not appear to offer any additional immunostimulatory effect.



Source: Atsmon *et al.*, 2014

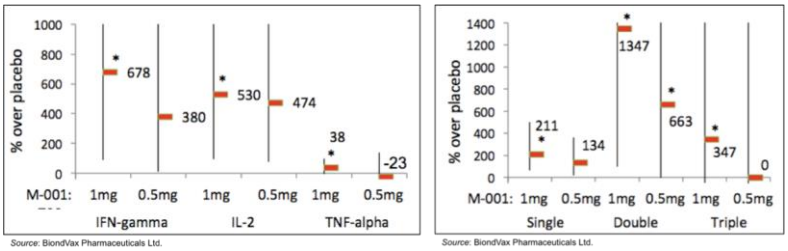
In 2015, a new 'Swiss' epidemic influenza strain (H3N2: A/Switzerland/9715293/13) emerged that did not exist in 2011, which was when the BVX-005 trial took place and the participants in the trial were immunized with M-001. Blood serum samples from the participants in the BVX-005 trial were exposed to the 'Swiss' influenza strain, with results showing that greater than 60% of the M-001 vaccinated group had seroprotection against this new Swiss strain, compared to only 10% of those immunized with just the seasonal vaccine. This suggests that M-001 may offer a broader, long-lasting immune response not just to strains currently in existence, but to future strains that do not even exist yet!



Source: BiondVax Pharmaceuticals, Ltd.

BVX-007: In 2017, BiondVax announced results from the company's Phase 2b clinical trial of M-001. The trial, which was funded through a grant from the European Union and was conducted in conjunction with the European UNISEC Consortium, enrolled a total of 219 participants aged 18 to 60 years. Each participant received two injections of 0.5 mg M-001, 1.0 mg M-001, or placebo prior to a partial dose of avian H5N1 pandemic vaccine.

The trial hit both primary endpoints for safety and immunological response. To test for immunological response, T cell activation was measured in *in vitro* assays through the release of the cytokines interleukin (IL)-2, interferon (INF)-γ, and tumor necrosis factor (TNF)-α. The following figure on the left shows that statistically significant T cell activation was found in participants that received 1.0 mg M-001 when compared to the placebo group. The following figure on the right shows that the there was a significant increase in T cells that expressed two cytokines, which have been shown to be functionally superior to single-cytokine producing T cells (Kannanganat *et al*., 2007).



Source: BiondVax Pharmaceuticals Ltd.

The study's secondary endpoint evaluated antibody response to avian H5N1 pandemic vaccination. In one of the four H5N1 strains tested there was a statistically significant increase in antibody response in those receiving M-001.

Valuation

We are very excited for the topline results of the Phase 3 trial for M-001, which we anticipate before the end of October 2020. This is a massive inflection point for the company and we anticipate all companies with a stake in the influenza market to be paying very close attention to the results. Positive results will likely lead to a regulatory filing in the E.U., however we anticipate some type of bridging study will likely be necessary before filing for approval in the U.S. Ultimately, with positive results we would not be surprised to see BiondVax be acquired by a larger pharmaceutical company. We have made no changes to our model and the valuation remains at $81 per share.

PROJECTED FINANCIALS

BiondVax Therapeutics, Ltd.	2019 A	Q1 A	Q2 A	Q3 E	Q4 E	2020 E	2021 E	2022 E
M-001 (Universal Vaccine)	$0	$0	$0	$0	$0	$0	$0	$45
YOY Growth		-	-	-	-			
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth		-	-	-	-			
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$45**
YOY Growth		-	-	-	-			
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$3
Product Gross Margin		-	-	-	-			
Research & Development	$19.9	$5.3	$3.4	$5.5	$5.7	$19.9	$22.0	$25.0
General & Administrative	$2.8	$0.3	$1.2	$1.0	$1.2	$3.7	$4.0	$30.0
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($22.7)	($5.6)	($4.6)	($6.5)	($6.9)	($23.6)	($26.0)	($13.0)
Operating Margin		-	-	-	-			
Non-Operating Expenses (Net)	($8.9)	$4.6	($7.5)	$0.0	$0.0	($3.0)	$0.0	$0.0
Pre-Tax Income	($31.6)	($1.0)	($12.1)	($6.5)	($6.9)	($26.6)	($26.0)	($13.0)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($31.6)**	**($1.0)**	**($12.1)**	**($6.5)**	**($6.9)**	**($26.6)**	**($26.0)**	**($13.0)**
Net Margin		-	-	-	-			
Reported EPS	**($0.09)**	**($0.00)**	**($0.03)**	**($0.01)**	**($0.01)**	**($0.06)**	**($0.06)**	**($0.03)**
Basic Shares Outstanding	326.7	408.6	454.4	460.8	460.8	446.1	460.0	470.0
Basic ADS Outstanding	8.2	10.2	11.4	11.5	11.5	11.0	11.5	11.8

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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